The New England
Journal of Medicine

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Volume 247 JULY 10, 1952 Number 2

ACCIDENTS COMPLICATING PELVIC SURGERY IN WOMEN*

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THE danger of accidents occurring during pelvic surgery in women is ever present, but the great advances in surgical technic, especially during the last quarter of a century, have been responsible for reducing these complications to a considerable degree. This has been brought about by better exposure of the operative field, by a suitably long incision, by careful and meticulous dissection before the structures are clamped and cut, by protecting the contiguous organs by proper walling off with moist gauze pads and by the complete relaxation of the abdominal wall and its contents, through the improved methods of anesthesia in vogue at the present time.

The accidents may be divided into those that occur during abdominal pelvic surgery and those that complicate surgery by the vaginal route. In either case this may be immediate or late.

IMMEDIATE ACCIDENTS COMPLICATING ABDOMINAL PELVIC SURGERY

Ureterovaginal Fistula

This complication usually accompanies the operation of panhysterectomy, especially the radical abdominal panhysterectomy for carcinoma of the cervix. Injury to the ureter may occur in one of three ways: directly, during the operation; by interference with the blood supply of the ureter in its extensive dissection during the course of the radical operation for carcinoma of the cervix; or by the application of a ligature around the ureter during ligation of the uterine vessels. Urinary leakage appears immediately after direct injury, whereas it occurs late when there is sloughing of an area in the ureter by interference with its blood supply or by its ligation. In the last condition the fistula usually appears above the ligature. Direct injury to the ureter may be avoided by ascertaining its location prior to the application of clamps or ligatures on the uterine vessels. While doing a difficult hysterectomy for any type of pathology, I have insisted that if there is any doubt about the position of the ureter this structure should always be dissected and kept in sight during the operation. As one's experience increases in the performance of pelvic surgery, he is more careful to preserve an adequate blood supply to the ureter, and, by exposing it, to avoid the danger of placing a ligature around it while the uterine vessels are being tied. If either ureter is injured during pelvic surgery it may be anastomosed over a catheter or by side-to-side anastomosis; it may be transplanted into the fundus of the bladder; in rare cases it may be transplanted into the sigmoid; and finally, it may be brought out through the skin in the lumbar region as a temporary measure until something else may be decided on.

Vesicovaginal Fistula

The bladder may be injured directly during its separation from the cervix and the vagina; it may be cut with the dissecting scissors or torn if blunt dissection is attempted. The bladder may also be injured by the sloughing of an area in which there has been interference to the blood supply during an extensive dissection of this viscus, and it may be injured by running a stitch through it while the vaginal cuff is being sutured. This accident may not occur if the bladder is sufficiently mobilized and if it is pushed away from the needle by the assistant each time it is passed through the vaginal cuff. The sloughing of a small area of the bladder as a result of interference with its blood supply is not so easy to prevent, since this condition is not recognized until urinary leakage takes place a number of days after operation. The only serious factor in injury to the bladder is the failure to recognize it. If the lesion is discovered and sutured immediately with fine catgut and the bladder is placed on constant drainage, healing is assured in most cases.

Injuries to the Rectum, Sigmoid and Small Intestine

These injuries to the bowel, large or small, usually occur while its adhesions in the pelvis are being liberated, commonly when operations for endometriosis or chronic pelvic inflammatory disease are being performed. Management of these complications may consist of suturing the rent with or with-

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Read at a sectional meeting of the American College of Surgeons, Quebec City, Quebec, February 18 and 19, 1952.

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out a temporary enterostomy while healing is taking place or resecting the involved area of the intestine with a suitable anastomosis, this being followed by the administration of the appropriate antibiotic.

Hemorrhage

Hemorrhage in the pelvis during operation may occur from the ovarian vessels or from the uterine vessels, due to the slipping or breaking of a clamp before the vessels are tied, to the slipping of a ligature or to the rupture of a brittle calcified uterine artery. The ovarian artery or vein is seldom lost during operation; rarely a small hematoma may form in the infundibulopelvic ligament if the ligature has not been applied tightly enough. This may be avoided if so-called pulley sutures are used in tying these vessels. If the accident has occurred, the layers of the infundibulopelvic ligament are separated, the blood clot is evacuated and the offending vessel is picked up and tied. In my experience it has never been necessary to ligate the ovarian artery at its origin at the aorta. *Per contra*, the retraction of the uterine artery after its rupture or the slipping of its ligature may present a more difficult problem. A large hematoma forms between the leaves of the broad ligament, the ureter is in the way and much time may be wasted in trying to find the retracted artery. I prefer to expose the hypogastric artery at its origin and apply a ligature there, thus easily controlling the bleeding, which may assume serious proportions should too much time elapse.

Late Accidents Complicating Abdominal Pelvic Surgery

Secondary Hemorrhage

This may be due to the slipping of a ligature and appear a few hours after operation, or it may be caused by the sloughing of the tissues and be discovered at a later date. The symptoms of shock and blood loss become apparent. Supportive treatment is administered to the patient, who is fortunate if she is in a hospital equipped with an adequate blood bank. When her condition is brought to its optimum state the abdomen is reopened and the offending vessel is found and ligated. If this is not possible the ligature is applied above the origin of the offending vessel, as in the case of the uterine artery when the hypogastric artery is ligated. The abdomen is closed quickly, frequently with through-and-through nonabsorbable sutures in order to save time, the patient is treated for shock and the blood loss replaced by transfusion.

Infection

Infection may occur at the time of operation and may not manifest itself until some time later, or it may develop during the convalescence. Infection in the pelvis takes the form of a pelvic abscess, a broad-ligament abscess or thrombophlebitis, pyemia and septicemia. Pelvic abscess is evacuated through the cul-de-sac of Douglas by posterior colpotomy; a broad-ligament abscess is evacuated extraperitoneally by an incision in the groin and elevation of the conjoined tendon, which permits entering the abscess without entering the peritoneal cavity. Certain broad-ligament abscesses that point toward and to the side of the cul-de-sac of Douglas may be reached through this avenue. Thrombophlebitis, pyemia and septicemia are treated appropriately by means of vein ligation, including the ligation of the vena cava when indicated, and the administration of antibiotics and sulfonamides. This form of treatment has made it possible to save many lives that could not have been saved a number of years ago.

Phlebothrombosis and Thromboembolism

Thrombosis and embolism, although not strictly surgical accidents, are complications that must be considered. These distressing late events in pelvic surgery, which are due to stagnation of blood, injury to blood vessels and infection, may be prevented in many cases. The control of infection has been brought about by the use of the antibiotics. Injury to the blood vessels may be minimized by gentle manipulation of the tissues and by the judgment and technic of the surgeon. Early ambulation has played an important role in preventing the stagnation of blood, and femoral-vein ligation, prophylactic and therapeutic, has proved of considerable value. In a paper presented recently at the seventy-fifth annual meeting of the American Gynecological Society, Dr. J. P. Pratt of Detroit stressed prevention by preoperative care. He stated that the problem begins before operation and continues through operation and during the postoperative period. As methods he emphasizes the allaying, on the evening before operation, of the fear of anesthesia, of being unsexed, of premature aging and so forth; the avoidance of heavy narcosis and hypnosis before and after operation; the proper selection of anesthesia, expertly administered and no deeper than necessary; gentle technic during operation, with no useless pressure on the viscera, no trauma from undue retraction and meticulous hemostasis; no unnecessary postoperative narcosis or hypnosis; early ambulation; and maintenance of the patient's morale at a satisfactory level. In following this advice we cannot avoid reducing the incidence of this distressing late complication.

Intestinal Obstruction

Intestinal obstruction, which is also rather a complication of pelvic surgery than an accident, may be largely prevented by careful peritonealization, by burying the stumps of the infundibulopelvic and round ligaments between the leaves of the broad ligaments in the performance of hysterectomy, by covering the raw areas in the pelvis with the bladder peritoneum and by bringing the

sigmoid into the pelvis before the small intestine is allowed to come down to that area. In certain cases, when the peritoneum has been sacrificed in the separation and division of adhesions, a satisfactory peritonealization may be obtained by roofing over the pelvis with the sigmoid, suturing it to the peritoneum of the pelvic wall on each side and to the bladder peritoneum anteriorly. In many cases, when signs of intestinal obstruction have appeared, the passage of the Miller–Abbott tube and the use of the Wagner suction apparatus will keep the bowel empty and allow the edema of the intestine to subside and the bowel to resume its function. This failing, the abdomen should be reopened, the adherent loop of bowel freed and bands of adhesions liberated. In certain cases it may be necessary to resect the involved loop of bowel, to anastomose the bowel and to resort to transfusions and antibiotics as necessary.

Immediate Accidents Complicating Vaginal Pelvic Surgery

Urinary Fistulas

Vesicovaginal fistula is more common after vaginal than after abdominal pelvic surgery. *Per contra*, ureteral injuries resulting in fistula are much less common since, in the performance of vaginal hysterectomy, the ureters are raised out of the way with the bladder. Moreover, the ureters are seldom exposed vaginally except in the performance of the Schauta radical vaginal hysterectomy, an operation that has never been popular in this country. A vesicovaginal fistula occurring during the course of a vaginal operation is usually easily repaired, and with the aid of constant bladder drainage it heals readily. When injuries to the ureters occur they are handled in much the same manner as in abdominal pelvic surgery.

Rectovaginal Fistula

This condition may occur as a result of direct injury to the rectum during the performance of vaginal plastic surgery, especially colpoperineorrhaphy. It is more likely to happen if previous operations have been performed in this area and the rectum is firmly adherent. Even then, sharp scalpel or scissors dissection of the rectum may prevent this accident, which is most commonly caused by blunt gauze dissection. The suture of the rent in the rectum with fine catgut and the approximation of the perineal muscles over the suture line will seal the area and will, as a rule, allow satisfactory healing.

Hemorrhage

Hemorrhage of a serious nature is seldom encountered during vaginal plastic surgery. It may occur during the performance of a vaginal hysterectomy through the slipping of a ligature on the uterine artery, an accident that I have avoided by resorting to pulley sutures in ligating all vessels during this operation. If the uterine artery is lost, the simplest way of stopping the hemorrhage is to make an abdominal incision and ligate the hypogastric artery of the corresponding side.

Late Accidents during Vaginal Plastic Surgery

Hemorrhage

Secondary hemorrhage may occur from sources other than the uterine artery. It may be the result of infection or the sloughing of the edges of the vaginal flaps if the sutures have been knotted too tightly. Such hemorrhages are generally controlled by vaginal gauze packing. Occasionally it is necessary to apply a small amount of ferric subsulfate solution (Monsel solution) to the area by placing it on the end of the vaginal gauze pack that is introduced against the bleeding area, or by oxycel and the gauze pack. Secondary hemorrhage may also occur after such operations on the cervix as trachelorrhaphy or amputation, through the premature absorption of the catgut sutures. The employment of forty-day No. 1 chromic catgut will greatly reduce the danger of this accident. It sometimes becomes necessary to apply a suture around a bleeding vessel. A gauze pack placed against the cervix causes sufficient pressure to control cervical bleeding in most cases.

Infection

Infection, which may take place at the time of operation during vaginal plastic surgery and which manifests itself at a later date, customarily remains localized to the pelvis and drains itself *per vaginam*. Vaginal preparation before these operations should always be gentle. Such agents as pHisoHex and solution of aqueous Zephiran, which are antiseptic but nonirritating, serve this purpose admirably. The administration of the antibiotics for about the first two postoperative days as a prophylactic measure may prevent many of these infections. Maintenence of a normal blood level, by means of blood transfusions, is also helpful. In vaginal hysterectomy, if there is oozing from the tissues, a small Penrose-tubing drain should be inserted and left in place for three or four days. A dry field is essential to prompt and satisfactory healing. Thrombophlebitis, pyemia and septicemia, which are of rare occurrence after such surgery, should be treated along the lines described under "Abdominal Pelvic Surgery."

Statistics

A review of my personal records from January 1, 1946, to January 1, 1951, reveals 1879 women operated on during this period. In this group 128 patients had operations listed as "miscellaneous," which consisted of operations on the breast, gallbladder operations, hemorrhoidectomies and so forth, and were eliminated from this study. This

left 1751 consecutive pelvic operations, as follows: 432 in 1946, 383 in 1947, 346 in 1948, 329 in 1949 and 261 in 1950.

There were 6 accidents in 1946, 7 in 1947, 4 in 1948, 1 in 1949 and 3 in 1950. There was therefore a total of 21 accidents in a group of 1751 consecutive patients, or 1.1 per cent.

The 21 accidents involved the urinary bladder in 10 cases, the ureters in 4 cases, the small intestine in 2 cases, the large intestine in 2 cases, perforation of the uterus in 1 case and infection in 2 cases. These are reported herewith in brief abstracts.

During the course of the operations on these 1751 consecutive patients the ureters were dissected in 55 in order to prevent injury to them during a total hysterectomy. Femoral- and saphenous-vein ligations were performed on 40 patients, 38 preoperatively and 2 postoperatively.

The ages of the 21 women who had accidents varied between twenty-three and sixty years, the average being forty-one years. There was no mortality in this group of 1751 patients, and all complications were overcome by appropriate treatment.

Case Reports

The following cases are listed according to their anatomic location:

Bladder, 10 Cases

Case 1. A small injury occurred during the performance of a vaginal hysterectomy. It was sutured immediately in layers and healing was entirely satisfactory.

Case 2. This patient had had a previous supravaginal hysterectomy, a left salpingo-oöphorectomy and a right salpingectomy at another hospital. She was operated on because of pain in the right ovary, a right oöphorectomy being performed. The ovary was adherent. During dissection of the right ureter, a small injury to the bladder occurred, which was sutured in layers, with satisfactory healing.

Case 3. A previous Beuttner operation (fundic hysterectomy, bilateral salpingectomy, suture of the ovaries to the round ligaments and bladder advancement) had been performed on this patient because of pelvic inflammatory disease. Subsequently a total hysterectomy and bilateral oöphorectomy were performed. The bladder was adherent and was injured during separation. The injury, which was small, was sutured in layers; healing was entirely satisfactory.

Case 4. Operation was performed on this patient because of severe pelvic endometriosis. It consisted of lysis of adhesions, total hysterectomy, bilateral salpingo-oöphorectomy and dissection of both ureters. A bladder tear, 4 cm. in length, occurred at the fundus of the bladder; it was sutured in layers and healed satisfactorily.

Case 5. This patient had had two previous cervical cesarean sections; a fundal myoma, a long cervix and pelvic endometriosis were present, the bladder being adherent. Total hysterectomy and bilateral salpingo-oöphorectomy were performed. The bladder injury was sutured in layers, with satisfactory healing.

Case 6. This patient also had had two previous cervical cesarean sections and an appendectomy; she had extensive pelvic adhesions. Total hysterectomy and left salpingo-oöphorectomy were performed. A bladder injury occurred and was sutured in layers. Healing was entirely satisfactory.

Case 7. Fundic hysterectomy and appendectomy had previously been performed elsewhere on this patient. There was now an adherent dermoid cyst of the left ovary with extensive intestinal and omental adhesions. The operation consisted of lysis of adhesions, left oöphorocystectomy and right oöphorectomy. A small bladder injury was sutured in layers and healing was satisfactory. (This patient had had a previous radical mastectomy for carcinoma of the left breast.)

Case 8. A Beuttner operation had previously been performed on this patient for pelvic inflammatory disease. She had also had an appendectomy. Subsequently she developed multiple myomas of the uterus for which total hysterectomy and bilateral oöphorectomy were performed. The bladder was adherent; during its separation a small injury occurred, which was sutured in layers, with satisfactory healing.

Case 9. This patient suffered an injury at the fundus of the bladder during the performance of a low transverse cervical cesarean section. Dilatation and currettage, Olshausen suspension of the uterus and appendectomy had previously been carried out; the bladder was adherent to the anterior abdominal wall and was opened in opening the peritoneum. It was sutured in layers and healing was satisfactory.

Case 10. Three previous pelvic laparotomies had been performed on this patient, who now had partial intestinal obstruction and myomas of the uterus. The bladder was adherent at the fundus of the uterus, the tubes and ovaries having been previously removed. The operation consisted of lysis of adhesions and total hysterectomy. The bladder was injured during its separation; it was sutured in layers and healing was satisfactory. Resection and lateral anastomosis of the small intestine for partial intestinal obstruction were performed.

Ureters, 4 Cases

Case 1. A total hysterectomy was performed, with excision of a remnant of the right ovary, which was adherent to the right ureter. The right ureter was injured during excision of the ovary; anastomosis of the ureter was performed, with satisfactory healing.

Case 2. Pelvic inflammatory disease was present in this patient, a small colon-bacillus abscess involving both tubes and ovaries having resulted from a vaginal hysterectomy. A mass containing both tubes and ovaries was excised. An injury occurred to the left ureter to which the mass was adherent; anastomosis of the ureter was performed, with satisfactory healing and preservation of kidney function.

Case 3. The right ureter was dissected during the performance of a total hysterectomy, bilateral salpingo-oöphorectomy and appendectomy. Extravasation of urine was noted on the fourth postoperative day. Lumbar and intraperitoneal drainage was instituted, and six blood transfusions — a total of 2090 cc. — were given. Satisfactory recovery resulted.

Case 4. This patient had "frozen pelvis" and endometriosis; a previous fundic hysterectomy and appendectomy had been performed elsewhere. The bladder had been sutured to the top of the remaining uterus. Lysis of extensive adhesions was performed and a normal right ureter dissected; because of dense adhesions the left ureter had also to be dissected in order to remove the left adnexa; in doing this the ureter was frayed for a distance of 2 cm. It could not be implanted in the fundus of the bladder, which it did not reach, nor could it be anastomosed. The patient's condition having become precarious and the right kidney and ureter being normal the left ureter was cut between ligatures. The patient was given blood transfusions and treated for shock, after which she made a good recovery. The left kidney underwent silent atrophy.

Small Intestine, 2 Cases

Case 1. This patient, with cholelithiasis and marked obesity, had had 3 previous pelvic operations. Her operation consisted of lysis of adhesions and presacral neurectomy. An injury occurred to the ileum, which was sutured transversely in three layers. Healing was satisfactory.

Case 2. This patient had polypoid carcinoma of the cervix, Stage I, and multiple *myomata uteri*. The ileum was adherent to the scar of a previous right inguinal herniotomy. Operation consisted of a total hysterectomy, bilateral salpingo-oöphorectomy and appendectomy. The serosa of the ileum was injured in separating it from the adhesions. Transverse suture of the ileum was followed by intestinal obstruction. Resection of the loop of ileum with lateral anastomosis and Witzel enterostomy was performed, with good recovery.

Large Intestine, 2 Cases

CASE 1. This patient had a left intraligamentous cyst with intestinal and omental adhesions. Two pelvic operations had previously been performed; the cecum was very adherent. Operation consisted of a left salpingo-oöphorectomy. In separating the adhesions the cecum was injured. It was sutured, and healing was satisfactory.

CASE 2. This patient had myoma of the uterus, severe pelvic endometriosis and adhesions of the sigmoid and rectum to the posterior surface of the uterus. Operation consisted of total hysterectomy, bilateral salpingo-oöphorectomy and dissection of both ureters. Eight blood transfusions were given. A rent in the rectum was sutured and healing was satisfactory.

Perforation of Uterus, 1 Case

CASE 1. This patient had perforation of the uterine wall below a myoma of the uterus. The operation consisted of a supravaginal hysterectomy, a small wafer of cervix being left in, and bilateral salpingo-oöphorectomy. Healing was entirely satisfactory.

Infection, 2 Cases

CASE 1. Infection in the form of pelvic cellulitis occurred in this patient after vaginal hysterectomy and plastic surgery for third-degree prolapse. Treatment was conservative, consisting of penicillin administration and multiple transfusions; the patient made a good recovery.

CASE 2. This patient had a dilatation and curettage, cauterization of the cervix, lysis of omental adhesions, plication of the uterosacral ligaments and Olshausen suspension with silk. A silk stitch on the right was removed, and one on the left that was infected. She made a good recovery.

SUMMARY AND CONCLUSIONS

Accidents occurring during pelvic surgery have decreased markedly in the last quarter-century because of improvement in surgical technic, in preoperative and postoperative care and in anesthesia.

Blood transfusions, intravenous and parenteral administration of fluids and the employment of antibiotics and sulfonamides have also played an important role in the recovery of patients.

The accidents that occur during pelvic operations may be immediate or late and may complicate both abdominal and vaginal surgery.

Between January 1, 1946 and January 1, 1951, 1751 consecutive pelvic operations were performed on my private patients, with a total of 21 accidents. These were treated by various means, as indicated, and there was no mortality.

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PULMONARY FUNCTION IN CONVALESCENT POLIOMYELITIC PATIENTS*

II. The Pressure-Volume Relations of the Thorax and Lungs of Chronic Respiratory Patients

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BETTER understanding of the respiratory problems encountered, and improved facilities for the treatment of acute poliomyelitis patients with respiratory involvement have apparently decreased the mortality rate in the acute stages of this disease.[1] Reduction of mortality, coupled with the increased incidence of the disease, has resulted in an increasing accumulation of severely crippled patients whose continuation of life depends on respiratory assistance. In April, 1951, there were approximately 500 patients in the United States who required a body respirator or other breathing aid for at least a fraction of each day.[2] The majority of such patients have been treated singly in small hospitals, with the result that few physicians have had the opportunity of prolonged and extensive experience with them.

The recent establishment of a respirator center under the administration of the Children's Medical Center has made possible the collection of data in a moderate number of cases. Attention has been particularly directed to an assessment of the rate and extent of recovery of pulmonary function following severe respiratory insufficiency and to an analysis of the changes in physical properties of the lungs and thorax. It was hoped that such studies would yield information of value not only in quantitating the degree of impairment but also in providing a yardstick for evaluation of therapeutic measures and for prediction of the extent of recovery.

The present report is concerned with alterations of the mechanics of breathing in such cases. Other aspects of the pulmonary-function studies in these patients have been reported separately.[3]

The normal mechanics of breathing involve a changing point of balance between the opposing elastic force of the lungs tending toward collapse and the elastic and muscular forces of the thorax tending toward expansion. When the inspiratory muscles contract, the balance point shifts toward expansion, or inspiration. The release of the inspiratory force allows the point of balance to move back toward the original volume, thus producing an essentially passive expiration. In a patient with

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Aided by a grant from the National Foundation for Infantile Paralysis, Incorporated. These studies were carried on at the Mary MacArthur Memorial Respirator Unit, Wellesley Convalescent Home and Hospital, and the Children's Medical Center, Boston.

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respiratory-muscle paralysis, the inspiratory force is achieved by mechanically reducing the pressure around the body while the airway pressure remains at atmospheric level. The resulting pressure gradient shifts the balance point to a higher level of lung inflation. When the pressure around the body returns to atmospheric, the balance point returns to its original position as expiration occurs. The lung-volume change, or tidal volume, is related to the magnitude of the pressure difference produced by the respirator. Plotting a series of the lung-volume changes against the corresponding pressure differences defines the pressure-volume relations of the thoracopulmonic unit.

In the chronic respirator patient the clinical impression that relative thoracic fixation or "collapse" of the chest may be present suggests that the pressure-volume relations may be abnormal. Another impression is that pulmonary emphysema may develop in respirator patients. The determination of pressure-volume relations should clarify these clinical impressions and in addition should provide a measure of the effectiveness of therapeutic procedures designed to alter these relations.

The purpose of this paper is to present a technic for the determination of the pressure-volume relations of the thoracopulmonic unit in a paralyzed subject and to consider the usefulness of such data in relation to therapy.

Methods

Nine chronic respirator patients (Table 1) were studied; all had severe residual paralysis of six to eighteen months' duration. Their respiratory ability as measured by the vital capacity ranged from 200 to 1000 cc. and the expiratory reserve from 0 to 60 cc. The respirator was cycled at a constant rate for a given patient. The tank pressure was varied from 0 to 40 cm. of water below atmospheric pressure. The average respirator is capable of reducing the pressure about 25 cm. of water below atmospheric level. Further reduction of the negative pressure phase to −40 cm. of water was obtained by connecting the suction end of a tank vacuum cleaner to a porthole for a period of two or three breaths. The pressures were measured by the gauge on the respirator after it was checked for adequacy of response and accuracy. The experimental assembly is shown in Figure 1.

Table 1. *Physical Characteristics of Patients Studied.*

Name	Sex	Age	Height	Weight	Body Surface Area	Vital Capacity Observed	Vital Capacity Predicted
		yr.	*cm.*	*kg.*	*sq.meters*	*liters**	*liters*
R. D.	M	15	187	45.0	1.61	0.68	4.85
J. T.....	M	7	125	18.0	0.82	0.22	1.59
A. M.....	M	34	174	...	...	0.57	4.15
P. G.	F	15	163	31.5	1.25	0.52	3.03
D. M.	F	20	173	53.5	1.62	0.36	3.42
L. A.	M	28	188	55.5	1.75	0.46	4.60
N. D.	M	28	186	56.5	1.76	1.10	4.56
C. H.	F	16	173	45.5	1.52	0.30	3.49
K. M.....	M	44	173	54.0	1.58	1.84	3.93

*Volumes BTPS (37° and saturated at ambient barometric pressure).

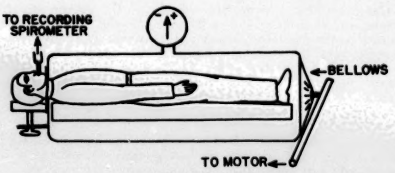

Figure 1. *Experimental Assembly for Study of Pressure-Volume Relations of the Thoracopulmonic Unit in a Patient with Poliomyelitis.*

Lung-volume changes were recorded on a Benedict–Roth type of spirometer (Fig. 2). Volumes were corrected to body temperature and pressure and saturated with water vapor (BTPS). They were then expressed as per cent of predicted total lung capacity in order to permit comparison among patients of different age, size and sex. The predicted total lung capacity was obtained by calculating the predicted vital capacity, using the regression equation of Baldwin et al.[4] for the adults and our own for the patients under 15 years[5] and assuming the vital capacity to be 75 per cent of the total lung capacity. This figure is in accord with lung-volume

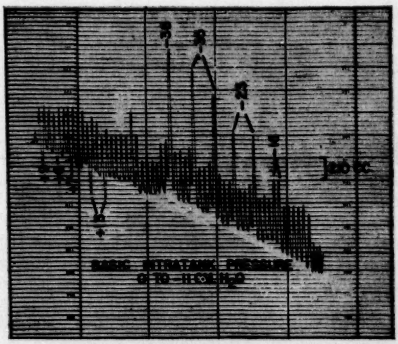

Figure 2. *Spirometric Record, Showing Changes in Tidal Volume at Different Pressures.*

Negative numbers refer to subatmospheric pressure peaks (inspiration); positive numbers indicate pressure peaks above atmospheric pressure (expiration).

data obtained in this laboratory and with the figures given by Baldwin et al.[4]

The relaxation volume, which is the same as the functional residual volume and represents the resting point of equilibrium between the opposing forces of the lungs and thorax, was measured by the closed-circuit helium-dilution method,[6] the average of duplicate determinations being used.

Before relating the intratank pressure changes to corresponding spirometer values, it was necessary to consider the possible errors involved. Because the intratank pressure was continuously changing and the tissues and airway offer resistance to volume change, it could be expected that the observed pressures in the tank would have passed their peak values before the lung-volume change was complete. The pressure difference between the tank and the mouth at the instant of complete volume change would therefore represent the *effective* ventilating pressure difference; thus in using the observed peak

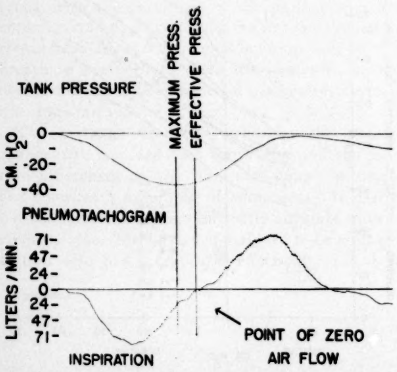

FIGURE 3. *Simultaneous Tracings of Intratank Pressure and Pneumotachogram, Showing Point of Maximum Effective Pressure as Demonstrated by Point of Zero Air Flow on Pneumotachogram.*

pressures in the comparison with volume changes, an error of some magnitude was introduced. In order to measure the seriousness of this error, the complete study was repeated with a more elaborate setup. In addition to the technic and equipment already described, the patient's air-flow pattern was recorded by means of a differential pneumotachograph with the resistance screen placed between the patient's airway and the spirometer. The recording was made on a direct-writing two-channel Sanborn oscillograph. Simultaneously, the intratank pressure was recorded on the second channel (Fig. 3). From this record the intratank pressure existing at the instant of maximum volume change (point of zero air flow on the pneumotachograph record) could be accurately determined. The error of the former method was small, as can be seen in Figure 4, in which the solid line represents the average curve for the 9 patients as measured by the simpler technic, and the dashed line represents the average curve for the same 9 patients as measured by the

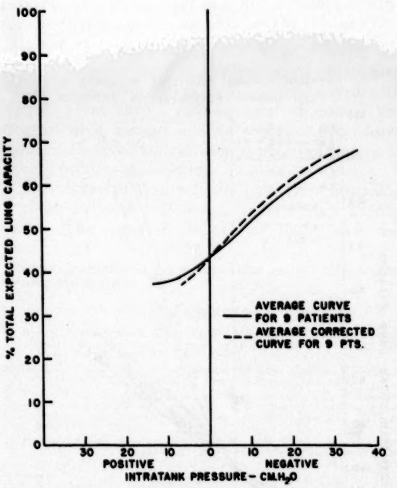

FIGURE 4. *Pressure-Volume Relation Measured in Resting Expiratory Position.*

second method described. This suggests that at the cycling rates utilized the resistive component of the applied pressure was small.

The lung-volume changes expressed as per cent of predicted total lung capacity have been plotted on the ordinate with the corresponding pressure differences on the abscissa (Fig. 5). The result was an S-shaped curve. On the average, 8 points were determined for each patient through which a curve was drawn. This method of drawing the curve is justified by other data. Several of the same patients were subsequently studied by the technic already described, but the tidal volumes were electrically recorded on the vertical axis of an oscilloscope and the corresponding pressure differences on the horizontal axis. This method gave the same S-shaped curves plotted by an infinite number of points as those obtained by the few points mentioned above. In order to compare the curves of the respirator patients with those of normal persons, two "relaxed" trained subjects were studied with the more exact technic. The results of these studies are plotted

on Figure 5; a curve was drawn by eye for these two subjects. Only the negative phase of the tank respirator was used, since it was thought that the positive phase yielded questionable results.

Results

In Figure 5 the relaxation lung volume, which is the volume corresponding to the zero or atmospheric-pressure line, has been arbitrarily set at 40 per cent of the predicted total lung capacity in order to simplify comparison of individual curves. The curves of the 9 poliomyelitis patients deviate from the normal and are remarkably similar to each other. This deviation toward the horizontal can be caused by several factors. If patients are able to resist the volume change to any degree, the curve will be tipped away from the vertical position in proportion to their ability to resist. On the inspiratory side of the zero pressure line this possibility can be minimized, for these patients have little or no active expiratory ability, their expiratory reserve at atmospheric pressure measuring from 0 to 60 cc., the majority being 0. The expiratory muscles are the ones needed to resist inspiration. The similarity of the curves strongly suggests that there was no interference, for it would be remarkable if they all resisted by the same amount.

However, the expiratory side of the curve (to the left of the zero pressure line) is open to considerable question because these patients did have limited inspiratory ability; they therefore could resist expiration more effectively than inspiration. The amount of interference is not measurable by the technic used.

An explanation of the abnormal pressure-volume relations of the lungs and chests of these patients cannot be made on the basis of present data. The decrease in distensibility could involve either the lungs, the chest or both and could be accounted for by pathologic processes that are known to occur. A separation of the two sets of factors depends on the measurement of intrapleural pressures simultaneously with the tank pressures and tidal volumes.

The curves as presented indicate the pressure gradient required to produce a given tidal volume and demonstrate that a given pressure gradient would produce a much greater tidal volume in a relaxed normal subject than in poliomyelitis patients. The repeated determinations of these curves could be used as a yardstick to measure the effect of certain therapeutic procedures. An increase in pul-

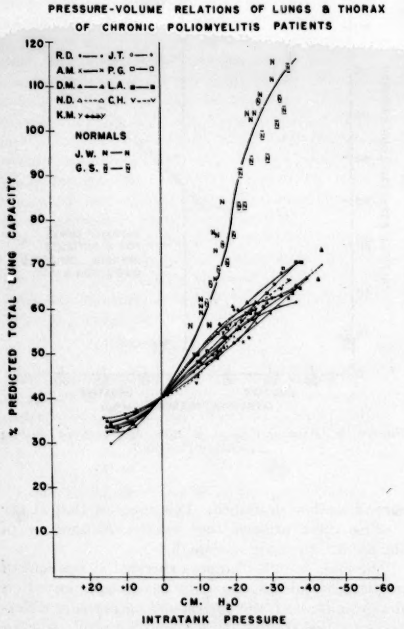

FIGURE 5. *Pressure-Volume Relations in 9 Patients with Poliomyelitis and 2 Normal Subjects.*

J. W. (N–N) and G. S. ($\overline{N}$–$\overline{N}$) represent the normal subjects; all others are patients.

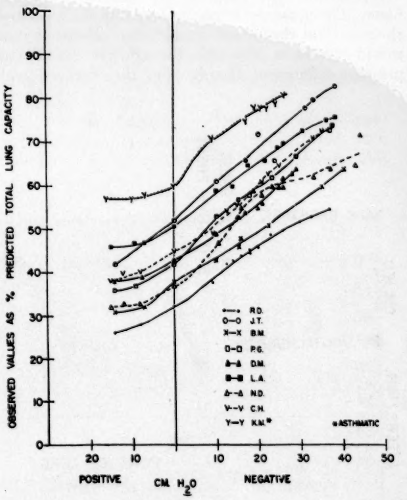

FIGURE 6. *Pressure-Volume Relations in 9 Patients with Poliomyelitis.*

monary or thoracic distensibility would be manifested by a more vertical slope of the curve. A change in the slope toward the horizontal would indicate a decrease in distensibility. The process of chest fixation could be plotted by following such measurements from the earliest time possible in the acute stage of the disease.

Figure 6 shows the curves for the same 9 poliomyelitis patients with their relaxation volumes placed in a position on the vertical scale as determined by the functional residual volume measurement. The volume below the point of cross-over on the zero pressure line represents the functional residual volume. It is interesting that all but one of the curves fall within a reasonable range of normal. The top curve, which is abnormally high, is that of a chronic poliomyelitis patient who also has chronic asthma and emphysema.

The fact that the relaxation volumes of these patients fall within normal limits indicates that their breathing position has changed little if at all. Thus there is no evidence that there has been collapse of the chest or the development of emphysema, with the exception of the patient who had chronic asthma. It further gives rise to speculation concerning how much muscle tone affects the breathing position, for here it appears to be unchanged despite the presence of marked respiratory-muscle paralysis.

The test, as described, whereby the volume changes are recorded on a spirometer and the pressure differences on the respirator gauge, is simple and requires a minimum of equipment. It carries but a small error and is sufficiently accurate to be of clinical value. Although it is designed to be used as a test, it also has therapeutic effects, by virtue of the fact that it produces an unusual amount of expansion of the chest. It is obvious that it is as important to put the paralyzed chest through a wide range of motion intermittently as it is to conduct similar physiotherapy on a paralyzed extremity.

Summary

The pressure-volume relations of the thorax and lung as a unit have been studied in 9 chronic respirator patients with difficulties due to poliomyelitis. The lung-volume changes were produced by cycling the tank respirator at different pressures. The data when plotted give a curve, the shape of which becomes a measurement of the degree of pulmonary distensibility. The curves have been compared with normal. The curves can be used to follow the progress of a patient and to evaluate procedures designed to mobilize and keep supple the thorax of chronic respirator patients.

The relaxation lung volumes have been measured in these patients and found to be within normal limits. The implications of this have been discussed.

We wish to express our appreciation for the technical assistance of Harriet A. Kriete.

References

1. Bower, A. G., Bennett, V. R., Dillon, J. B., and Axelrod, B. Investigation on care and treatment of poliomyelitis patients. *Ann. West. Med. & Surg.* 4:561-582, 1950.
2. Landauer, K. S. (Director of Medical Services, National Foundation for Infantile Paralysis, Inc.). Personal communication.
3. Ferris, B. G., Jr., Affeldt, J. E., and Whittenberger, J. L. Pulmonary function in convalescent poliomyelitic patients. I. Pulmonary subdivisions and maximum breathing capacity. *New Eng. J. Med.* 246:919-923, 1952.
4. Baldwin, E. deF., Cournand, A., and Richards, D. W., Jr. Pulmonary insufficiency. I. Physiological classification, clinical methods of analysis, standard values in normal subjects. *Medicine* 27:243-278, 1948.
5. Ferris, B. G., Jr., Whittenberger, J. L., and Gallagher, J. R. Maximum breathing capacity and vital capacity in male children and adolescents. *Pediatrics* (in press).
6. Gilson, J. C., and Hugh-Jones, P. Measurement of total lung volume and breathing capacity. *Clin. Sc.* 7:185, 1949.

THE INCIDENCE OF PRENATAL SYPHILIS AT THE BOSTON CITY HOSPITAL*

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BOSTON

IN A previous communication|| one of us reported on a retrospective analysis of congenital syphilis in patients under one year of age in Massachusetts, from 1946 to 1950 inclusive, in order to determine why congenital syphilis still continued to occur in spite of the following factors: a low prevalence rate of syphilis in this state: the premarital-examination law designed to screen for syphilis prospective couples before marriage and to provide treatment before the wedding of those found to have infectious syphilis; the prenatal-examination law requiring a blood test for syphilis at the first prenatal visit; a specific, effective and nontoxic antibiotic—penicillin; and the availability of good medical care.

In tracing the maternal past history of these infected children, this study showed that congenital syphilis occurred for the following reasons: 30 per cent of the mothers failed to seek prenatal care; 20 per cent had inadequate prenatal care; 17 per cent failed to complete treatment; 12 per cent became infected subsequent to the initial negative prenatal blood test; approximately 5 per cent had either a relapse or reinfection. Furthermore in 7 per cent of the cases there was believed to be an inadequate basis for the diagnosis of congenital syphilis, in 5 per cent the physician neglected to take the prenatal blood test, and in 3 per cent there was failure of apparently adequate treatment.

This study of congenital syphilis in Massachusetts was an analysis of our tragic failures. It left many questions unanswered. Therefore, a companion study was undertaken at the Boston City Hospital to provide an answer to the following five questions: What is the incidence and prevalence of syphilis in pregnancy at the Boston City Hospital? What is the incidence of prenatal syphilis developing subsequent to the initial negative prenatal blood test? How many mothers delivered at this large municipal hospital have had prenatal care? When in pregnancy did these mothers obtain prenatal care? What immediate effect did anesthesia have on the reaction of the blood test for syphilis?

PROCEDURE

From June 1, 1951, to October 21, 1951, each woman admitted in labor to the maternity service at the Boston City Hospital was given the customary obstetric examination and questioned concerning when and where prenatal care was obtained and the results of the blood tests.

When the patient was admitted, the upper half of the study form was completed by the admitting physician. After delivery, when the mother was returned to the maternity ward and within twenty-four hours of delivery, one of our technicians visited the ward and took blood samples for the Hinton test from all women who had been delivered since the technician's last visit. On Mondays, the blood sample was taken from mothers who had been delivered over the week end. Thus, blood for the Hinton test was obtained in most cases within forty-eight hours of delivery.

The Hinton test was performed on the collected samples and positive tests were immediately reported by telephone to the obstetric resident. In the meantime, the technician had completed the lower half of the study form and mailed it to the Division of Venereal Diseases of the Massachusetts Department of Public Health. Each day as the forms arrived, they were coded and the data punched on 80-column I.B.M. statistical cards.

Patients with positive or doubtful Hinton tests were followed for diagnostic study as syphilis suspects. The blood test was repeated and a quantitative Hinton test was performed. The height of the reagin titer has been helpful in differentiating falsely and truly positive tests for syphilis.

The patient was questioned concerning a history of syphilis as well as of other venereal diseases. If she had had syphilis, inquiries attempted to establish the date of her infection, whether or not she had been treated and where, the amount and type of treatment and treatment received during this pregnancy. Information was sought concerning infection and treatment in her husband and her other children, if any.

In the meantime, both the central registry files in the Division of Venereal Diseases and the hospital files were examined for any record of the patient. It was particularly important to verify the patient's diagnostic and treatment record in order

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||Fiumara, N. J. Congenital syphilis in Massachusetts. *New Eng. J. Med.* 245:634-640, 1951.

that the adequacy of treatment prior to or during this pregnancy might be determined.

When careful questioning and examination, including repeated blood tests, failed to establish a diagnosis of syphilis, particularly when the serologic reactions were consistently of low titer or doubtful and the patient had no history of syphilis, a Treponema-immobilization test (TPI) was performed.

The infants were watched carefully during the neonatal period and were followed for at least three months before a diagnosis of "not infected" was made. Fathers and siblings were also examined.

Age, Race and Marital Status of Mothers

From June 1, 1951, to October 21, 1951, 1005 women were delivered and blood-tested for syphilis within forty-eight hours after delivery at the Boston City Hospital (Table 1). There were 731 (72.7 per cent) white and 271 (27.0 per cent) Negro mothers; 44 (4.4 per cent) were single and 949 (94.4 per cent) were married. The average age of the mothers was 26.7 years.

The average age of the 731 white mothers was 27.1 years; 21 (2.9 per cent) of these mothers were single and 703 (96.2 per cent) were married.* Of the 271 Negro women, 21 (7.7 per cent) were single and 246 (90.8 per cent) were married.* Their average age was 25.6 years.

Prenatal Care

There were 836 (83.2 per cent) mothers who gave a history of having had prenatal care, whereas 169 (16.8 per cent) failed to report such care.

The average age of the mothers having prenatal care was 26.6 years in contrast to an average age of 27.0 years for those who had had none.

The percentage of those having had prenatal care did not differ appreciably in the white and Negro groups, being 83.0 per cent for the white and 84.5 per cent for the Negro mothers. However, there were significantly more Negro single mothers (16, or 76.2 per cent) who had received prenatal care in contrast to the single white women (10, or 47.6 per cent) who had received it. There was no such difference for the married groups by race.

Of these 836 mothers who gave a history of prenatal care, 74 gave no record of having had a prenatal blood test. Therefore, if these 74 mothers are added, as they should be, to the 169 patients who had no prenatal care, there will be a corrected total of 243 (24.2 per cent) patients who had either no prenatal care or no objective evidence of a prenatal blood test.

An additional 27 patients definitely stated that no prenatal blood test had been taken; these were mostly patients who had been cared for by private physicians. Another correction, therefore, must be made to our already corrected total, making 270 (26.9 per cent) patients who did not have prenatal care or any objective evidence of a prenatal blood test.

Curiously enough, repeated pregnancies did not influence a mother to seek prenatal care, and in this series of cases the proportion of mothers with prenatal care was approximately the same irrespective of whether they were pregnant for the first time or had had repeated pregnancies.

When did these mothers seek prenatal care? The average time was when they had been 26.2 weeks pregnant. More instructive is the answer to this question by trimesters. Of the 679 women who had had prenatal care and for whom the dates of their last period were available, 55 (8.1 per cent) reported during the first trimester, 273 (40.2 per cent) in the second trimester and 351 (51.7 per cent) during the third trimester (Table 2). Essentially the same

Table 1. *Proportion of Mothers Having Prenatal Care, by Race and Marital Status.*

Marital Status	All Mothers						White Mothers						Negro Mothers					
	Total		Prenatal Care		No Prenatal Care		Total		Prenatal Care		No Prenatal Care		Total		Prenatal Care		No Prenatal Care	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Single	44	4.4	27	3.2	17	10.0	21	2.9	10	1.6	11	8.8	21	7.7	16	7.0	5	11.9
Married	949	94.4	800	95.7	149	88.2	703	96.2	591	97.5	112	89.6	246	90.8	209	91.3	37	88.1
Widowed	1	0.1	0	0.0	1	0.6	1	0.1	0	0.0	1	0.8	0	0.0	0	0.0	0	0.0
Divorced	5	0.5	4	0.5	1	0.6	2	0.3	1	0.2	1	0.8	3	1.1	3	1.3	0	0.0
Separated	4	0.4	4	0.5	0	0.0	3	0.4	3	0.5	0	0.0	1	0.4	1	0.4	0	0.0
Not stated	2	0.2	1	0.1	1	0.6	1	0.1	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
Totals	1005	100.0	836	100.0	169	100.0	731	100.0	606	100.0	125	100.0	271	100.0	229	100.0	42	100.0

*These percentages do not add up to 100 because the widowed, divorced and separated mothers were omitted.

Table 2. *Trimester in Pregnancy of First Prenatal Visit, by Race.*

Trimester in Which Blood Test Taken	All Women Tested		White Women Tested		Negro Women Tested	
	No.	%	No.	%	No.	%
First	55	8.1	34	6.9	21	11.4
Second	273	40.2	207	41.9	66	35.9
Third	351*	51.7	253	51.2	97	52.7
Totals	679*	100.0	494	100.0	184	100.0

*Includes 1 case in which the race of the patient was unknown.

percentages applied to both primiparous and multiparous women.

Analysis by race and marital status did not affect this basic trend of late prenatal care, in that the majority of the mothers appeared for prenatal care, irrespective of race and marital status, during the third trimester, with a decreasing proportion reporting to the physician during the second and the first trimesters, in that order.

The need for re-emphasizing early prenatal care is obvious.

Results of Prenatal Test

Of the 735 cases for which prenatal blood test reports were available, 11 (1.5 per cent) were positive, 1 (0.1 per cent) was doubtful and 1 (0.1 per cent) was unsatisfactory. No record of a repeated blood test could be found for those patients who had doubtful or unsatisfactory tests.

Analysis by race shows that there were 3 (0.6 per cent) positive tests for the white mothers and 8 (4.0 per cent) for the Negro patients. The one doubtful test was in a white woman.

Of a total of 23 single mothers who had prenatal blood tests made, 1 (4.3 per cent) was positive and 1 doubtful. The positive test was in a Negro mother and the doubtful test in a white one.

In the married group, there were 10 (1.4 per cent) positive Hinton tests, 3 of them (0.6 per cent) in white and 7 (3.7 per cent) in Negro women.

What was the incidence of syphilis in the mothers at the time that they had their prenatal care? How many cases of syphilis, both new and old, were discovered during the prenatal period?

There were no cases of seronegative primary syphilis in this group, so the diagnosis of past or present syphilis was established on the basis of either a history of the disease in addition to a positive or doubtful blood test or a history of exposure together with repeated positive laboratory tests, and in one case by the presence of secondary lesions and a doubtful blood test.

How many cases of syphilis were there in all? Eleven mothers had positive prenatal blood tests. Of these, 7 (63.6 per cent) had been diagnosed and had received some treatment prior to this pregnancy. The remaining 4 (36.4 per cent) had been diagnosed for the first time during the pregnancy. There was, however, one doubtful blood test also. This was diagnosed at the patient's first prenatal visit, clinically and by dark-field examination, as secondary syphilis. There was no record of a repeat blood test. Thus the prevalence of old and new syphilis in the mothers receiving prenatal care, including the prenatal blood test for syphilis, was 1.2 per cent. The incidence of new infection was 0.7 per cent; of these cases 1 was found in a single white mother, 1 in a married white patient and 3 in married Negro women.

Post-Partum Blood Tests

As mentioned above, all mothers delivered at the Boston City Hospital were given a blood test for syphilis within forty-eight hours after delivery. This made it possible to determine how many mothers had developed detectable syphilis since their initial negative prenatal blood test and to calculate the incidence and prevalence of syphilis in that group of mothers who had had no prenatal care or blood test. Finally, a true incidence and prevalence rate of detected syphilis could be computed for this group of 1005 mothers who had been delivered at the Boston City Hospital during this time interval.

Table 3. *Results of Prenatal Blood Tests and Ultimate Post-Partum Diagnosis.*

Results of Prenatal Blood Test	No. of Cases	Ultimate Post-partum Diagnosis						
		Not Infected	Early Syphilis		Late and Late Latent Syphilis		Congenital Syphilis	
			Previously Known	Not Previously Known	Previously Known	Not Previously Known	Previously Known	Not Previously Known
Positive	11	1	3	1	2	2	2	—
Doubtful	1	—	—	1	—	—	—	—
Unsatisfactory	1	1	—	—	—	—	—	—
Negative	722	717	1	2	1	1	—	—
No test made	27	26	—	—	—	—	1	—
Unknown	243	236	2	2	1	2	—	—
Totals	1005	981	6	6	4	5	3	—

At post-partum examination, 17 (1.7 per cent) mothers were found to have had positive blood tests, and 8 (0.8 per cent) patients had doubtful tests. Of these 17 mothers with positive tests, 8 had had positive tests during prenatal care and the remaining 9 had positive blood tests at post-partum examination.

What was the prenatal history of these 9 patients? There was a history of a negative prenatal blood test in 3. In 1 patient no prenatal blood test was taken or recorded, and in the remaining 5 there had been no prenatal care (Table 3).

At post-partum examination 8 doubtful blood tests were found. Examination showed that 6 of

these 8 mothers had had prenatal care. In 3 mothers the prenatal blood test was positive, in 2 the blood Hinton was negative and in 1 the test was doubtful.

What was the diagnosis in those mothers with positive and doubtful tests? It will be recalled that 8 of the 17 mothers with post-partum positive tests also had positive prenatal Hinton tests and were diagnosed at the time of their prenatal care as having either old or recent infection. The remaining 9 mothers were diagnosed as follows:

The 3 mothers with negative prenatal blood tests were found to have been infected. Two of them had had latent syphilis adequately treated prior to this pregnancy, and in the third a diagnosis of latent syphilis was established after delivery. The mother who had had prenatal care but denied that a blood test had been taken (no record of the test could be found) was discovered to have had adequately treated congenital syphilis. There now remain 5 mothers who had no prenatal care. Three of these mothers were infected and treated before this pregnancy, 1 for secondary syphilis and the other for latent syphilis. The remaining 2 cases represent diagnoses established after delivery.

Thus, for the 17 patients with post-partum positive blood tests, all were found to have been infected (Table 4). Of these, 14 were diagnosed before delivery (in 2 cases the diagnosis was established during this pregnancy; the diagnosis in the remaining 12 was made prior to this pregnancy). There were 3 patients in whom the diagnosis was not established until after delivery. One of these patients had had a negative prenatal blood test and therefore probably represents an infection acquired during pregnancy but after the initial prenatal test. The other 2 had had no prenatal test and the diagnosis was established after delivery.

There were 8 doubtful blood Hinton tests. Subsequent tests and investigations established a diagnosis of syphilis in all but 1. In the 6 who had had prenatal care, 3 had positive prenatal tests and therefore represent cases of treated syphilis with falling titers that had not reached seronegativity. In 2, the prenatal blood tests were negative. After the first doubtful post-partum tests, repeated tests fluctuated from doubtful to low-titered positive — the history was not helpful. The probability of the diagnosis was therefore established by means of the Treponema-immobilization test. The sixth case was a patient with secondary syphilis treated at the time of her prenatal visit. Two patients had no prenatal care. Repeated tests and the Treponema-immobilization test established the diagnosis of latent syphilis in 1; the other patient had a negative blood test at the fifth month post partum, at which time she also had a negative Treponema-immobilization test.

Thus, as a result of the 17 positive and 8 doubtful post-partum blood tests, a diagnosis of syphilis was established in the 24 patients, a prevalence rate of 2.4 per cent.

Of these 24 cases, 13 represent old and treated cases of syphilis; the remaining 11 were diagnosed either prenatally or after delivery, an incidence rate of newly discovered syphilis of 1.1 per cent. Of these new cases of syphilis, 4 were diagnosed prenatally and 7 after delivery. Only 1 was thought to have been infected after the initial negative prenatal blood test.

The distribution of these 24 infected cases was as follows: 8 were white and 16 were Negroes. Of the 8 white mothers, 1 was single and 7 were married. In the group of 16 Negro mothers, 1 was single, 14 were married and 1 was divorced.

There were 11 mothers who were recently diagnosed cases of syphilis. Of these, 4 were white and 7 Negro. Of the white women, 1 was single and 3 were married. In the 7 Negro mothers, 6 were married and 1 was divorced.

TABLE 4. *Results of Prenatal and Post-Partum Blood Tests.*

Results of Prenatal Blood Test	No. of Cases	Results of Post-Partum Blood Tests		
		Positive	Doubtful	Negative
Positive	11	8	3	—
Doubtful	1	—	1	—
Unsatisfactory	1	—	—	1
Negative	722	3	2	717
No test made	27	1	—	26
No information about blood test	243	5	2	236
Totals	1005	17	8	980

Congenital Syphilis

One of the happy features of this study is that there were no cases of congenital syphilis in the newborn. Normally with untreated primary or secondary syphilis in pregnant women, one would expect that half the infants born would be either premature, neonatal deaths or stillbirths; the other half would be infected with congenital syphilis. The probability that a normal full-term infant will be born of these mothers is extremely small.

If the mother had untreated early latent syphilis, there would be an expected prematurity rate of 20 per cent, with an additional 4 per cent of the infants being neonatal deaths and 10 per cent stillbirths. Approximately 40 per cent of the infants born will have congenital syphilis and 20 per cent of the infants will escape, being normal full-term nonsyphilitic babies.

With late untreated syphilis, one would find that about 10 per cent of the infants would have congenital syphilis; another 10 per cent would be stillbirths, about 9 per cent premature and about 1 per cent neonatal deaths. The last two outcomes, prematurity and neonatal deaths, are in approxi-

mately the same proportion as one would expect from normal noninfected pregnant women.

All the mothers in this series had single births. However, of the 1005 infants delivered, 119 (11.8 per cent) were prematurely born. Our criterion of prematurity was that of a live-born infant with a period of gestation of less than 37 weeks. When the period of gestation was unknown or unreliable, an infant's weight at delivery of 5½ pounds or less was indicative of prematurity.

Of the 24 mothers who had either old or recent syphilitic infection, 6 (25 per cent) had premature infants. Prematurity occurred twice as frequently in the recently diagnosed mothers (36.4 per cent) as in the mothers who had been diagnosed prior to this pregnancy (15.4 per cent). It will be recalled that the diagnosis of syphilis was made in 7 mothers after delivery. These mothers, therefore, represented untreated syphilis in pregnancy; in 4 (57.1 per cent) prematurity occurred. Although the prematurity rate in the infected group is higher than in the noninfected mothers, no valid conclusions can be drawn, because of the small number of cases involved.

All infants born of infected mothers were followed clinically and serologically for at least three months. One infant had a positive Hinton test at the fifty-first day and a negative blood test on the seventy-second day (no treatment had been given). Later tests were also negative. There were no clinical or x-ray evidences of congenital syphilis. The original positive test was accounted for on the basis of passive reagin transfer.

There were 2 neonatal deaths in the infants of infected mothers, neither of which was due to congenital syphilis.

Blood-Test Reaction and Anesthesia

Of the 1005 mothers delivered, the records of anesthesia are available on 997. Of these, 500 received ether inhalation, 428 spinal anesthesia, 1 intravenous anesthesia and 78 none. Six positive and 5 doubtful blood Hinton tests were found among the mothers receiving ether inhalation. The 6 positive tests and 4 of the doubtful cases have already been accounted for on a basis of recent or old infection; one doubtful blood test was found in a mother who subsequently had negative tests. There were also 6 positive and 3 doubtful blood tests occurring in those mothers receiving spinal anesthesia; these also have been accounted for on a basis of recent or old infection. Four mothers who had no anesthesia had a positive blood test, and in one mother for whom a record of anesthesia was not available a positive blood Hinton test was found.

Therefore, in this series of patients, anesthesia, whether of inhalation or of spinal type, caused no false positive blood tests within forty-eight hours of delivery.

Summary

From June 1, 1951, to October 21, 1951, 1005 women were delivered and blood-tested for syphilis at the Boston City Hospital within forty-eight hours of delivery. Twenty-four were found to have been infected with syphilis. The mean age of the mothers was 26.7 years, an average that was not materially affected by race or marital status. Four per cent were single.

A little more than 72 per cent of the mothers were white; 2.9 per cent of these were single, whereas 7.7 per cent of the Negro mothers were single.

Based on history alone, slightly more than 16 per cent admitted having had no prenatal care. On investigation, however, 24.2 per cent of the series had no objective record of prenatal care or a prenatal blood test. It was this group that contributed 8 (33.3 per cent) of the 24 mothers found to have been infected with syphilis.

In general, the proportion of white and Negro mothers receiving prenatal care was about the same.

Of the mothers who had prenatal care, 51.7 per cent consulted a physician for the first time at the third trimester, 40.2 per cent at the second trimester and 8.1 per cent at the first trimester. This pattern of late prenatal care was noted irrespective of the race and marital status of the women and, what is more important, regardless of whether this was the mother's first or tenth pregnancy.

Less than half the mothers ultimately found to be infected were diagnosed during the prenatal period. Nearly all would have been diagnosed prenatally if they had had prenatal care.

As a result of this study, it was found that 24 mothers had either old or recent syphilitic infection, a prevalence rate of 2.4 per cent. However, the incidence of newly discovered syphilis was 1.1 per cent. Only 1 patient was found probably to have been infected after the negative initial prenatal blood test. Twice as many Negro women as white women were found to be infected. Single women, either white or colored, comprised less than 10 per cent of the total infected group. Of definite interest is the fact that of the 24 women found to have been infected 7 (29.2 per cent) had had no prenatal care or prenatal blood test.

There were no multiple births in this series of 1005 mothers; however, 119 babies (11.8 per cent) were born prematurely. Prematurity occurred twice as frequently among mothers with recent or old infections as among the noninfected mothers. In addition, the prematurity rate was twice as frequent in the recently diagnosed syphilitic mothers; although the prematurity rate in the infected group is higher than in the noninfected women, no valid conclusions can be drawn because of the small number of cases involved. It was fortunate that no cases of congenital syphilis were found in this series. The blood test for syphilis was not adversely affected by anesthesia.

THE RELATION OF OBESITY TO MENSTRUAL DISTURBANCES*

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BOSTON

AMONG clinicians dealing with problems of reproductive physiology there is a widespread clinical impression that obesity is related to amenorrhea and perhaps other functional disorders of menstruation. Wharton's standard textbook of gynecology[1] lists obesity as commonly associated with amenorrhea. Duncan[2] mentions that various disturbances of menstruation, including dysmenorrhea, functional bleeding, amenorrhea and infertility, are frequently associated with obesity and that weight reduction can be effective in alleviating the menstrual disturbance. Other authors[3-8] indicate the not infrequent relation of obesity and menstrual disturbances, and Given[9] mentions attempts at weight reduction in obese women with amenorrhea as a therapeutic measure.

A careful search of the literature of the past twenty-two years discloses no systematic study of a large group of patients with menstrual abnormalities to determine the validity of this clinical impression. Armstrong and others[10] have commented on the need for studies on the relation of obesity to endocrine function. It is the purpose of this paper to present statistical evidence indicating a significantly increased incidence of obesity in patients with amenorrhea in comparison with a similar group of women without menstrual disturbances and to consider the possible relation of obesity to other types of functional disorders of reproduction.

METHODS

A group of patients in the New England Center Hospital and the Boston Dispensary with functional menstrual disturbances, including abnormal uterine bleeding, amenorrhea, premature menopause, habitual abortion and infertility, served as subjects for study. All patients with demonstrable pelvic abnormalities were excluded. The selected subjects ranged in age from sixteen to forty years. In each case the patient was subjected to thorough medical and gynecologic study. When indicated, determinations of follicle-stimulating hormone were made by the method of Klinefelter and Albright[11] and pregnanediol excretions by the Astwood method.[12] The diagnosis of obesity was made by reference to standard nomographs.[13] Only those patients who were 20 per cent or more over ideal weight were classified as obese. The patients, both obese and nonobese, were then grouped according to diagnosis, and the incidence of obesity in each category was determined.

A control group of 201 women patients from the same hospitals who had no menstrual disorders were interviewed. Only those with normal menstrual cycles were selected to serve as control subjects. Normal cycles were defined as menstruation occurring at intervals of twenty-three to thirty-five days with the duration of flow not exceeding eight days.[14, 15] Many of these patients were suffering from various medical disorders that were believed to have no significant bearing on the reproductive functions. The incidence of obesity was determined in this control group. As an additional control, the statistics of the Massachusetts Health Protection Clinic were used, and the incidence of obesity in a group of 730 women was determined.

Amenorrhea was considered to be present when menses had been absent for at least three months at the time that the patient was first seen. Those women whose amenorrhea was associated with serious systemic disease were excluded.

Functional uterine bleeding was accepted as a diagnosis when the menses were more frequent than every twenty-three days or when bleeding was prolonged for nine days or more and local or systemic causes of abnormal uterine bleeding had been excluded. Two conditions were required for classification of a patient as infertile: a year or more of barren marriage without contraception and an adequate semen specimen from the husband. Amenorrhea in the presence of a high follicle-stimulating-hormone determination in women below forty years of age was considered to be evidence of a premature menopause. Habitual abortion included those women who had had three or more miscarriages without successful completion of a pregnancy.

RESULTS

Of 100 patients with menstrual disorders that included amenorrhea, functional uterine bleeding, premature menopause, infertility and habitual abortion, 43 were obese in that their weight was 20 per cent or more over their calculated ideal weight. In the control group of women of similar age range but with normal menstrual periods, the over-all incidence of obesity was 13 per cent. This latter

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This study was aided by grants from the Hannah and Harry Posner Fund and the Charlton Fund.

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figure compares favorably with the 9.6 per cent incidence of obesity in women of the same age range in the file of the Massachusetts Health Protection Clinic.[16]

The 100 patients were classified by diagnosis, and the incidence of obesity in each group was determined (Fig. 1). It is of interest that 60 of the patients had amenorrhea and that 29 of these were

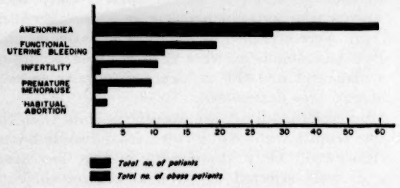

FIGURE 1. *Incidence of Obesity in Total Group in Each Category (Sixteen to Forty Years of Age).*

obese, an incidence of 48 per cent, which is significantly greater than the 13 per cent incidence in the control group. In 19 patients with functional uterine bleeding, the incidence of obesity was 58 per cent. In the remaining diagnostic categories, there were too few patients to provide adequate statistical data.

Of greater significance are the results obtained when the patients are divided into age groups of from sixteen to twenty-nine years (Fig. 2) and from thirty to forty years (Fig. 3). The fact that the

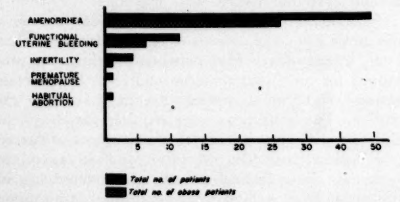

FIGURE 2. *Incidence of Obesity in Each Diagnostic Category (Sixteen to Twenty-Nine Years of Age).*

majority of the patients were between sixteen and twenty-nine years old increases the emphasis on obesity in this group because of the greater predisposition to the disease in older women. Forty-seven of the 60 patients with amenorrhea fell into the age range of sixteen to twenty-nine years; 26, or 55 per cent, were overweight. This figure is in striking contrast to the 7 per cent incidence of obesity in this age range in Control Group 1 and 8.8 per cent in Control Group 2.

In the age range from thirty to forty years, there were 13 patients with amenorrhea; 3, or 23 per cent, were obese. There were too few patients in the remaining categories to be of statistical significance. The incidence of obesity in the corresponding Control Group 1 was 18 per cent; in Control Group 2 it was 10 per cent. That obesity is more common in older women is substantiated by Control Group 1, in which the incidence rose from 7 per cent in the sixteen-to-twenty-nine-year age range to 18 per cent in the thirty-to-forty-year range, and by Control Group 2, in which the incidence rose from 8.8 per cent to 10 per cent — yet in the patients under study, obesity reached its peak incidence (55 per cent) in the younger age range as compared with only 23 per cent in the thirty-to-forty-year range.

Discussion

The results of this study indicate that there is an increased incidence of obesity in women with amenorrhea as compared with two control groups of women with normal menstrual cycles. That this is statistically valid can be demonstrated, the probability of this association's occurring by chance being 2×10^{-9}. There were insufficient data to

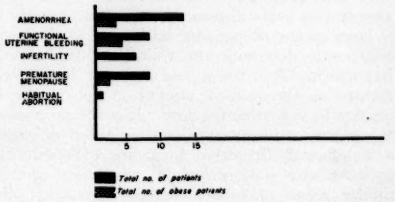

FIGURE 3. *Incidence of Obesity in Each Diagnostic Category (Thirty to Forty Years of Age).*

evaluate the incidence of obesity in other menstrual abnormalities, but the available evidence suggests that a correlation exists.

This demonstration of the association of these two symptoms cannot be interpreted as showing that there is a common etiologic factor, and it cannot be concluded from these results that obesity is a cause of amenorrhea. That in certain instances emotional disorders might be a factor in both obesity and amenorrhea remains unproved.

In animals, experimental hypothalamic lesions can be shown to cause obesity. Brobeck[17] has reviewed the mechanism of hypothalamic obesity. There is also increasing evidence of a close relation between the hypothalamus and the regulation of reproductive function. Dey[18] has shown that hypothalamic lesions in female guinea pigs may produce changes in the estrous cycle, genital atrophy and interference with secretion of luteinizing hormone. A clinical concept of hypothalamic amenorrhea has been presented by Klinefelter, Albright

and Griswold[11] and further commented on by Reifenstein.[19] In this syndrome, there is postulated an interference with the hypothalamic pituitary pathways that release luteinizing hormone. It is not inconceivable that in some instances both obesity and menstrual abnormalities might be manifestations of hypothalamic disorder. As long ago as 1921, Bailey and Bremer[20] expressed the opinion that obesity and sexual functions were related. Others,[21, 22] however, have thought that obesity and genital hypoplasia are not necessarily related, as certain hypothalamic lesions may produce one without the other. However, previous authors[2,9] have mentioned the effect of weight reduction in alleviating menstrual disorders, and in our series of obese women with amenorrhea there have been several instances of return of normal periods after weight reduction. These observations and the demonstration of a high incidence of obesity in amenorrhea suggest that a common factor may be found to be causally related to both clinical conditions. Further studies to determine the effect of weight reduction in women with amenorrhea are currently in progress.

Summary and Conclusions

The incidence of obesity in a group of 100 young women with functional menstrual disorders, infertility and habitual abortion was investigated. Forty-three per cent were found to be 20 per cent or more over their calculated ideal weight. Amenorrhea was the most frequent menstrual disorder, and 48 per cent of the patients with amenorrhea were obese in contrast to a 13 per cent incidence in a control group. The results, which are statistically significant, give factual proof to the clinical impression of the association of obesity and menstrual disturbances. The possibility of a hypothalamic origin of both obesity and amenorrhea is briefly discussed.

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References

1. Wharton, L. R. *Gynecology Including Female Urology.* 1027 pp. Philadelphia: W. B. Saunders Company, 1942. P. 164.
2. Duncan, G. *Disease of Metabolism.* 985 pp. Philadelphia: W. B. Saunders Company, 1942. Pp. 564, 585 and 586.
3. Ray, H. M. Obese patient: statistical study and analysis of symptoms, diagnosis and metabolic abnormalities: sex differences — treatment. *Am. J. Digest. Dis.* **14**:153-162, 1947.
4. Bayer, L. M. Build in relation to menstrual disorders and obesity. *Endocrinology* **24**:260-268, 1939.
5. Johnston, J. A. Nutritional problems of adolescence. *J. A. M. A.* **137**:1587-1589,1948.
6. Randall, L. M. Treatment of amenorrhea in young women. *Am. J. Obst. & Gynec.* **53**:453-458, 1947.
7. Novak, E. Gynecologic problems of adolescence. *J. A. M. A.* **117**: 1950-1952, 1941.
8. Day, L. A., and Smith, P. L. Reproductive career of women with ovarian dysfunction. *Am. J. Obst. & Gynec.* **60**:93-100, 1950.
9. Given, W. P., Gause, R. W., and Douglas, R. G. Rational therapy for secondary amenorrhea. *New Eng. J. Med.* **243**:357-362, 1950.
10. Armstrong, D. B., Dublin, L. I., Wheatley, G. M., and Marks, H. H. Obesity and its relation to health and disease. *J. A. M. A.* **147**: 1007-1014, 1951.
11. Klinefelter, H. F., Albright, F., and Griswold, G. C. Experience with quantitative test for normal or decreased amounts of follicle stimulating hormone in urine in endocrinological diagnosis. *J. Clin. Endocrinol.* **3**:529-544, 1943.
12. Rogers, J., and Sturgis, S. H. Pregnanediol excretion in normal women. *J. Clin. Endocrinol.* **10**:89-100, 1950.
13. Nomograph for determining percent above or below ideal weight. Fed. Sec. Agency, Public Health Service, Division of Chronic Disease.
14. Rock, J. Menstruation: its disorders and their treatment. *New Eng. J. Med.* **233**:817-824, 1945.
15. Goldzieher, J. W., Henkin, A. E., and Hamblen, E. C. Characteristics of normal menstrual cycle. *Am. J. Obst. & Gynec* **54**:668-675, 1947.
16. Massachusetts Health Protection Clinic. Unpublished data.
17. Brobeck, J. R. Mechanism of development of obesity in animals with hypothalamic lesions. *Physiol. Rev.* **26**:541-559, 1946.
18. Dey, F. L. Evidence of hypothalamic control of hypophyseal gonadotropic functions in female guinea pig. *Endocrinology* **33**:75-82, 1943.
19. Reifenstein, E. C., Jr. Psychogenic or "hypothalamic" amenorrhea. *M. Clin. North America* **30**:1103-1114, 1946.
20. Bailey, P., and Bremer, F. Experimental diabetes insipidus. *Arch. Int. Med.* **28**:773-803, 1921.
21. Brooks, C. McC., Lambert, E. F., and Bard, P. Experimental production of obesity in monkey (Macaca mulatta). *Fed. Proc.* **1**:11, 1942.
22. Hetherington, A. W., and Ranson, S. W. Relation of various hypothalamic lesions to adiposity in rat. *J. Comp. Neurol.* **76**:475-499, 1942.

MEDICAL PROGRESS

SURGERY OF THE HEART AND GREAT VESSELS (Concluded)

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THE GREAT VESSELS

Some of the most important accomplishments of cardiovascular surgery are those having to do with the correction of congenital anomalies of the major vessels close to the heart and the creation of vascular shunts for the relief of certain cardiac anomalies. Although the technical problems involved in dealing with the vessels are simpler than those presented by the necessities of intracardiac surgery with a bloodless heart, it should be pointed out that every effort should be made to establish the diagnosis early in life so that the necessary corrective operation can be performed during childhood, before the size and rigidity of the chest and the presence of degenerative alterations of the vessels and other complications have occurred to make such surgery more difficult and more dangerous. Earlier diagnoses are being made not only as a result of the awareness on the part of the clinician of the possibilities of obtaining surgical relief but also because of the availability of newer diagnostic methods such as angiocardiography for visualization of the anatomic pattern and cardiac catheterization for study of the intracardiac and pulmonary oxygen saturation and pressure relations.

Patent Ductus Arteriosus

The first of the congenital anomalies of the major vessels to be corrected by surgical means was persistent patency of the ductus arteriosus. Since the original success of Gross and Hubbard,[48] interest has centered principally around the technical aspects of efforts to interrupt the flow of blood through this vessel. Some difference of opinion exists as to whether division of the ductus or ligation in continuity should be employed. Gross maintains, as originally suggested in 1944,[49] that complete surgical division should be carried out in all cases. There is no question that division of the ductus eliminates completely the possibility of recanalization and aneurysmal dilatation. It must be recognized, however, that in the hands of the majority of surgeons this procedure presents greater risk of hemorrhage from technical errors and a higher death rate than the operation of ligation without division. Many surgeons, therefore, have adopted the view that in the majority of cases ligation, often with multiple suture ligatures as advocated by Blalock,[50] is preferable. It is interesting in this connection that Touroff, who has had an unusually large experience with interruption of the patent ductus, particularly in the difficult cases of subacute bacterial endarteritis and endocarditis, has always employed the multiple-ligature method with excellent results.[51] He has pointed out that failure to secure permanent occlusion after ligation of the ductus may be attributed to incomplete occlusion by a ligature that has not been tied tightly enough.[52] In the experience of the Massachusetts General Hospital only one proved instance of recanalization has been observed in a series of 66 cases. It was observed at the operation on this patient that the ductus was so short that it comprised hardly more than a fistulous opening between the aorta and the pulmonary artery. With the newer technics and instruments now available, a ductus such as this should be divided instead of relying on ligation in continuity. The special ductus clamps of Potts and Smith are designed to improve the safety of this procedure.[53]

It should be pointed out that all such procedures are much safer and more easily accomplished in children than in adults. This is partly because of their smaller size and the greater retractability of the chest wall, but also because of the condition of the ductus itself; it is usually relatively longer and has a more pliable arterial wall in children than in adults. In patients with an unusually short ductus or in those who may require a secondary operation because of recanalization, the modification of the Potts–Smith aorta clamp devised by Freeman and his associates[54] may be employed to accomplish the division of the ductus. The use of this clamp permits control of the danger of hemorrhage from the aortic side so that the ductus may be divided with greater safety.

It is to be hoped that henceforth the diagnosis of patent ductus arteriosus will be made early in life so that advantage can be taken of the greater ease, safety and permanency of result obtained by performing the operation during childhood.

Ordinarily the diagnosis of patent ductus arteriosus can be readily made on the basis of a characteristic continuous murmur. That this murmur may not be present has been clearly shown. The reason for its absence has been suggested by cardiac-catheterization studies showing that in certain cases of patent ductus, pulmonary artery

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pressures, particularly the diastolic, may equal systemic arterial pressures. When no pressure differential exists in diastole, presumably no significant flow will occur and the diastolic component will be lost. Since such pressure relations are to be expected in the presence of a large defect and are probably related to severe vascular damage to the lungs, the importance of making an early diagnosis of such atypical cases is obvious.[55]

Double Aortic Arch with Annular Constriction of the Trachea and Esophagus

The clinical picture resulting from constriction of the esophagus and trachea by a congenital vascular ring due to the persistence of an early embryonic arrangement of the aorta as a double vessel has been recognized for many years. The possibility of surgical division of the constricting ring was mentioned as early as 1933 by Sprague, Ernlund and Albright.[56] The first reported case of division of such a ring was that of Gross in 1945.[57] The second case was that of a patient operated on at the Massachusetts General Hospital ten days later.[58] Since then, other reports have appeared in the literature having to do chiefly with the diagnosis and the descriptions of variations of the anatomic pattern of the vessels. The operation of division is relatively simple. The smaller of the vascular components should be divided, thus allowing the circulation to be carried efficiently by the larger vessel. Fortunately, the smaller vessel, which sometimes consists merely of a band of tissue resulting from obliteration of the lumen, usually lies anteriorly and is relatively accessible for division. In the majority of instances a thoracotomy on the left side provides ready access to the vessel to be divided. Sometimes, however, the right side is preferable, as in a case already reported in which the vascular pattern proved to be actually like the mirror image of the usual arrangement.[58] The clue to this situation lies in observing the side on which the aorta descends. This is usually the left, but if it should be the right, the vessel to be divided is more easily found through a right thoracotomy.

Bahnson and Blalock[59] report an interesting experience where a patient with a double aortic arch had also the tetralogy of Fallot. At operation it was possible to take advantage of the opportunity to relieve both conditions by division of the anterior aortic arch with ligation of the proximal end and the performance of an anastomosis between the distal end and the left pulmonary artery.

A related anomaly sometimes encountered is the situation in which the right subclavian artery arises from the first portion of the descending aorta just beyond the termination of the arch, whence it passes obliquely behind the esophagus to reach the right side of the base of the neck. Surgical division of the anomalous artery, however, is almost never necessary because of the rarity of the occurrence of symptoms (dysphagia lusoria). In fact, although this anomaly occurs more frequently than a double aortic arch with annular constriction, it is rarely discovered in the living except during the course of examinations for other causes of symptoms or during operations within the mediastinum.

Transposition of the Aorta and the Pulmonary Artery

As pointed out by Hanlon and Blalock, the survival of infants born with transposition of the aorta and pulmonary artery depends on the coexistence of some type of communication between the two sides of the heart, which is of course necessary because the systemic and pulmonary veins retain their normal position.[60] Theoretically the situation might best be corrected by producing a transposition of the veins, but thus far this cannot be accomplished. Attempts to interchange the pulmonary artery and the aorta await the perfection of an artificial heart and lung to by-pass the circulation. Even then difficulties might arise from the fact that the coronary arteries would continue to receive venous blood from the right ventricle. Thus far a degree of improvement has been achieved in some patients by creating a large interauricular septal defect and in some by the creation of a right-left shunt by end-to-end anastomosis of a pulmonary artery with a major branch of the aorta.[61]

Coarctation of the Aorta

One important advance in the surgery of the great vessels is the operation for coarctation of the aorta described independently in 1945 by Crafoord and Nylin[62] and by Gross.[63] Two types of this congenital anomaly are recognized. One, called the infantile type because it is usually incompatible with life and thus rarely seen in an adult, consists of a narrowing or obliteration of the aorta proximal to the location of the ductus arteriosus, which remains patent. Often almost the entire aortic arch is involved. The circulation distal to the atretic or stenosed segment takes place through the pulmonary artery and the patent ductus, producing cyanosis and clubbing of the lower extremities while the upper extremities may remain reasonably normal. No collateral circulation is developed. Attempts to correct the anomaly in infants have been almost universally unsuccessful. A few successes have been obtained in older patients using aortic homografts. The adult type consists of a stricture at some point beyond the origin of the left subclavian artery, either distal to or just at the level of the aortic attachment of the ductus (or ligamentum) arteriosus. Variations in the degree of the atresia, the length of the narrowed segment and its proximity to the origin of the left subclavian artery occur and are of great importance to the surgeon from the point of view of the technic required.

It should be pointed out that the diagnosis of coarctation of the aorta can be made easily by clinical investigation and roentgen study of the chest. With an increased awareness of the occurrence of the condition, therefore, all cases should be discovered during childhood, when the operation can be performed more easily and safely. In early years (six to twelve) the ease of access and the pliable condition of the aorta add greatly to the safety of the procedure. Although successful operations are nowadays carried out on adults, in a few cases even as old as forty years, the tendency to early development of arteriosclerotic changes in the vessel wall proximal to the lesion, in addition to the greater difficulty of operation through the adult chest wall, makes the procedure more hazardous the older the patient is allowed to become before surgery is undertaken.

The operative mortality is low: close to 0 in children and under 10 per cent in adults, as reported by Burford.[64] The results are excellent, with restoration of normal pulsations in the once pulseless arteries of the lower extremities and a reduction of arterial blood pressure of the upper extremities, usually to normal levels.

Certain variations in the anatomic characteristics and location of the narrowed segment of aorta have great bearing on the possibility of a successful completion of the operative procedure. Thus if the coarctation is too close to the left subclavian artery, it may be impossible to resect it in such a manner as to leave enough proximal end to perform the anastomosis. In this instance the left subclavian artery may be divided and the end turned down, as suggested by Blalock and Park.[65] If the length of aorta below the subclavian artery is sufficient for the performance of an anastomosis and if the narrow segment is short, a resection and end-to-end restoration of continuity of the aorta can be readily accomplished. Fortunately, this situation usually prevails. If, on the other hand, as sometimes happens, the narrowed segment is long, the two ends of the aorta cannot be brought together. It then becomes necessary to substitute an aortic graft, as practiced originally by Gross and associates.[66, 67] Obviously this method requires the facilities of an aortic-graft bank, with special attention to the procurement of specimens under aseptic precautions and their preservation by specialized technics. Such cases cannot be dealt with, therefore, in the average hospital.

Because of the importance of accurate foreknowledge of the exact nature of the coarctation in a patient for whom operation is contemplated, radiologic visualization of the aorta is desirable. If this cannot be accomplished by ordinary angiocardiography, in which concentrated Diodrast or a similar substance is injected rapidly into a peripheral vein, it may be necessary to resort to retrograde aortography. Under these circumstances concentrated Diodrast is injected into the arch of the aorta by means of a large catheter passed in a retrograde direction through the ulnar, brachial and subclavian arteries. This method is not without hazard to the upper extremity, and this has led several surgeons to prefer retrograde injection through a common carotid artery without the use of a catheter. It is of the greatest importance when injecting concentrated Diodrast into a proximal aorta to guard against rapid flooding of the cerebral circulation with the material and against the ever-present danger of cerebral air embolism.

Vascular Shunts for the Relief of Stenosis of Cardiac Valves

The pioneering work of Blalock and Taussig[68] resulting in the operation devised to improve the circulation through the pulmonary circuit in the tetralogy of Fallot is well known and need not be reviewed here. This work, however, has stimulated a renewed interest in this and related cardiac anomalies, resulting not only in the development of new technical methods but also in a clarification of knowledge about their application in relation to the varying types of deformity encountered.

Pulmonary Stenosis or Atresia

It should be remembered that a deficiency of blood flow to the lung from stenosis of the pulmonic valve is usually associated with other anomalies of the heart and that the choice of operation for its correction, either a shunt between the aorta and a pulmonary artery or a direct attack on the constriction itself, depends on the anatomic situation in each case.

Although other variations of abnormal pattern may occur, the most frequent is the combination of anomalies known as the tetralogy of Fallot. In the beginning, following the work of Blalock and Taussig[68] and of Potts, Smith and Gibson,[69] an aorta-to-pulmonary-artery shunt was always employed. Brock,[70] Blalock and Kiefer,[71] Potts,[72] Bailey[73] and others have pointed out, however, that in certain cases of tetralogy of Fallot a diaphragmatic valvular stenosis exists rather than a long infundibular stenosis and that enlargement of the stenotic valvular orifice by transventricular instrumentation with an especially devised knife or dilating instrument (Brock[70] or Potts[72]) is preferable to the creation of an artificial patent ductus arteriosus.

In the case of a "pure" or "isolated" pulmonic stenosis where there is no associated interventricular defect and where there may be no cyanosis until late, there is no question of the superiority of a direct attack on the stenotic valve over creation of an aortic-pulmonary-artery shunt.[74] In point of fact, the latter procedure is generally inadvisable, since it effects only a minimal increase in the passage of unoxygenated blood to the lung and then only if the patient is already cyanotic, usually on

the basis of a right-to-left shunt through a patent interauricular septum.

In the majority of cases that are unsuitable for valvulotomy two types of surgical procedure are available for the creation of a shunt to increase the pulmonary blood flow. The surgeon should be prepared to perform either one. It is then possible to complete the operation in any case by using a left thoracotomy approach. Usually it will be found (especially in children) that a direct anastomosis can be made between the aorta and the left pulmonary artery by the method of Potts, Smith and Gibson.[69] This has the advantage of simplicity and ease of accomplishment without the drawbacks of interrupting the circulation of a large branch of the aorta such as the subclavian or, even worse, the innominate or common carotid arteries as required by the Blalock method. In some instances, however, either because of anatomic variations in the relations of the vessels or because of their size (as in adults) it may be difficult or impossible to create a direct anastomosis between the aorta and the pulmonary artery. It then becomes necessary to utilize one of the large branches of the aorta, preferably the subclavian.

With regard to the end results of the operation in patients with tetralogy of Fallot one awaits the passage of time to obtain an answer. Obviously many lives have been saved among children who would have died without the procedure, and the operation provides a measure of palliation that in many cases is striking. Thus far, however, not enough time has elapsed to ascertain what degree of normal living may be possible for these patients as they reach adult years.

Mitral Stenosis

Brief mention might be made of a procedure evolved to relieve the hypertension within the pulmonary circuit in certain cases of pure mitral stenosis characterized by the occurrence with crippling frequency of attacks of pulmonary edema. This operation consists of the creation of a shunt between a branch of the right inferior pulmonary vein and the azygos vein.[75, 76] Although as a method of palliation in carefully chosen cases the results were gratifying at first, the coincidental revival of the method of relieving the same difficulty by a direct attack on the stenotic mitral valve has supplanted it as the method of choice in the majority of cases. Of those patients operated on before the operation of valvulotomy became widely used, there was striking relief in the majority of cases, with rehabilitation and freedom from attacks of pulmonary edema for as long as several years in some cases. Some of these patients, however, have begun to have recurrence of attacks of pulmonary edema; 3 (out of 11 who were greatly relieved by the shunt) have been reoperated on, this time by valvulotomy. The method, therefore, though promising as a stop-gap procedure, can now be abandoned in the majority of cases in favor of a direct attack on the mitral valve itself.

Aneurysm of the Aorta

Progress in the treatment of aneurysm of the aorta has been slow. Thus far the methods most frequently employed are purely palliative. Both Blakemore[77] and Linton[78] have revived and improved the method of treatment, which consists of an attempt to produce clotting of the blood within the sac by stuffing it with fine wire. Blakemore's technic employs a wire that is insulated in such a way as to make it possible to pass an electric current through to increase the clotting within the sac ("electro-thermic coagulation"). He reports 8 cases of arteriosclerotic aneurysm of the abdominal aorta in which the result was successful, with complete occlusion of the aorta and the development of a collateral circulation. Linton has stressed the relief of pain induced by wiring the sac, even though in many cases ultimate rupture of the aneurysm may occur and life may not be much prolonged.

Another method used by certain surgeons consists of partial wrapping of the aneurysmal dilatation with cellophane, which stimulates an intense production of fibrous tissue, which it is hoped will in turn diminish the possibility of rupture. A recent success with this method was reported by Cowley, Sloan and Sullenberger,[79] who used polythene containing dicetyl phosphate, which is known to be the agent causing the fibrous-tissue reaction. The patient had a saccular aneurysm of the ascending aorta with erosion of the sternum. Complete obliteration was effected by a fibrous-tissue reaction induced by strips of polythene film used to encircle the neck of the sac. It is hardly ever possible, however, to surround the aneurysm completely with this material. Furthermore, it has been discovered that cellophane from some sources does not contain the reactive agent and causes little reaction, whereas that from others may have an intense effect.[80] This method therefore appears to have a limited usefulness.

Recent work on the preservation and employment of aortic homografts in the treatment of certain cases of coarctation of the aorta suggests that in some cases resection of aneurysmal segments of the aorta may become possible. Lam[81] has reported one case with survival for a period of several weeks. Further experience and animal experimentation may point the way to a more successful employment of this method under favorable circumstances.

Saccular aneurysms of the aorta may occasionally be excised surgically. Recently DeBakey[82] has been able to accomplish this in 2 cases of aneurysm of this type arising from the aortic arch.

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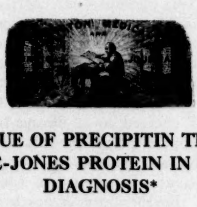
References

48. Gross, R. E., and Hubbard, J. P. Surgical ligation of patent ductus arteriosus. *J. A. M. A.* **112**:729-731, 1939.
49. Gross, R. E. Complete surgical division of patent ductus arteriosus: report of 14 successful cases. *Surg., Gynec. & Obst.* **78**:36-43, 1944.
50. Blalock, A. Operative closure of patent ductus arteriosus. *Surg., Gynec. & Obst.* **82**:113, 1946.
51. Touroff, A. S. W. Personal communication.
52. *Idem.* Discussion on "Complications of surgery of patent ductus arteriosus" by Dr. John C. Jones and "Complete division for patent ductus arteriosus" by Dr. Robert E. Gross. *J. Thoracic Surg.* **16**: 322-327, 1947.
53. Potts, W., Gibson, S., Smith, S., and Riker, M. Diagnosis and surgical treatment of patent ductus arteriosus. *Arch. Surg.* **58**:612-622, 1949.
54. Freeman, N. E., Leeds, F. H., and Gardner, R. E. Technique for division and suture of patent ductus arteriosus in older age group. *Surgery* **26**:103-108, 1949.
55. Myers, G. S., Scannell, J. G., Wyman, S. M., Dimond, E. G., and Hurst, J. W. Atypical patent ductus arteriosus with absence of usual aortic pulmonary pressure gradient and of characteristic murmur. *Am. Heart J.* **41**:819-833, 1951.
56. Sprague, H. B., Erhlund, C. H., and Albright, F. Clinical aspects of persistent right aortic root. *New Eng. J. Med.* **209**:679-686, 1933.
57. Gross, R. E. Surgical relief for tracheal obstruction from vascular rings. *New Eng. J. Med.* **233**:586-590, 1945.
58. Sweet, R. H., Findlay, C. W., Jr., and Reyersbach, G. C. Diagnosis and treatment of tracheal and esophageal obstruction due to congenital vascular ring. *J. Pediat.* **30**:1-17, 1947.
59. Bahnson, H. T., and Blalock, A. Aortic vascular rings encountered in surgical treatment of congenital pulmonic stenosis. *Ann. Surg.* **131**:356-362, 1950.
60. Hanlon, C. R., and Blalock, A. Complete transposition of aorta and pulmonary artery: experimental observations on venous shunts as corrective procedures. *Ann. Surg.* **127**:385-397, 1948.
61. Blalock, A., and Hanlon, C. R. Surgical treatment of complete transposition of aorta and pulmonary artery. *Surg., Gynec. & Obst.* **90**:15, 1950.
62. Crafoord, C., and Nylin, G. Congenital coarctation of aorta and its surgical treatment. *J. Thoracic Surg.* **14**:347-361, 1945.
63. Gross, R. E. Surgical correction for coarctation of aorta. *Surgery* **18**: 673-678, 1945.
64. Burford, T. H. Symposium on clinical surgery: coarctation of aorta and its treatment. *S. Clin. North America* **30**:1249-1158, 1950.
65. Blalock, A., and Park, E. A. Surgical treatment of experimental coarctation (atresia) of aorta. *Ann. Surg.* **119**:445-456, 1944.
66. Gross, R. E., Bill, A. H., Jr., and Pierce, E. C., II. Methods for preservation and transplantation of arterial grafts, etc. *Surg., Gynec. & Obst.* **88**:689, 1949.
67. Gross, R. E. Treatment of certain aortic coarctations by homologous grafts: report of 19 cases. *Ann. Surg.* **134**:752-768, 1951.
68. Blalock, A., and Taussig, H. Surgical treatment of malformations of heart in which there is pulmonary stenosis or pulmonary atresia. *J. A. M. A.* **128**:189-202, 1945.
69. Potts, W. J., Smith, S., and Gibson, S. Anastomosis of aorta to pulmonary artery: certain types in congenital heart disease. *J. A. M. A.* **132**:627-631, 1946.
70. Brock, R. C. Pulmonary valvulotomy for relief of congenital pulmonary stenosis: report of 3 cases. *Brit. M. J.* **1**:1121-1126, 1948.
71. Blalock, A., and Kiefer, R. F., Jr. Valvulotomy for relief of congenital valvular pulmonic stenosis with intact ventricular septum: report of 19 operations by Brock method. *Ann. Surg.* **132**:496-516, 1950.
72. Potts, W. J. Discussion of Blalock and Kiefer.[71]
73. Glover, R. P., Bailey, C. P., and O'Neil, T. J. E. Surgery of stenotic valvular disease of heart. *J. A. M. A.* **144**:1049-1057, 1950.
74. Potts, W. J., and Riker, W. L. Surgical treatment of pulmonary stenosis with intact interventricular septum. *Arch. Surg.* **62**:776-784, 1951.
75. Bland, E. F., and Sweet, R. H. Venous shunt for advanced mitral stenosis. *J. A. M. A.* **140**:1259-1265, 1949.
76. Sweet, R. H., and Bland, E. F. Surgical relief of congestion in pulmonary circulation in cases of severe mitral stenosis: preliminary report of 6 cases treated by means of anastomosis between pulmonary and systemic venous systems. *Ann. Surg.* **130**:384-397, 1949.
77. Blakemore, A. H. Progressive constrictive occlusion of abdominal aorta with wiring and electrothermic coagulation: one-stage operation for arteriosclerotic aneurysms of abdominal aorta. *Ann. Surg.* **133**:447-462, 1951.
78. Linton, R. R. Intrasaccular wiring of abdominal arteriosclerotic aortic aneurysms by "pack" method. *Angiology* **2**:485-498, 1951.
79. Cowley, R. A., Sloan, H. E., and Sullenberger, N. H. Successful repair of aortic aneurysm with sternal perforation. *J. Thoracic Surg.* **21**:159-163, 1951.
80. Yeager, G. H., and Cowley, R. A. Studies on use of polythene as fibrous tissue stimulant. *Ann. Surg.* **128**:509-520, 1948.
81. Lam, C. R. Resection of descending thoracic aorta for aneurysm. *Ann. Surg.* **134**:743-752, 1951.
82. DeBakey, M. Personal communication.

MEDICAL INTELLIGENCE



THE VALUE OF PRECIPITIN TESTS FOR BENCE-JONES PROTEIN IN EARLY DIAGNOSIS*

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THE need for a specific quantitative test for Bence-Jones protein has long existed. Most commonly employed are nonspecific chemical procedures, of which the electrophoretic is the most delicate. Even this technic, however, requires protein concentration in excess of 1 per cent for positive results. Therefore, chemical demonstrations of Bence-Jones protein in the urine or serum are a relatively rare event in the average hospital laboratory. Customarily thought of as occurring in about 65 per cent of cases of multiple myeloma and rarely in other conditions, the excretion of this protein is actually not as uncommon as it is generally considered to be. The rarity of this finding may well be an indication of the inadequacy of methods currently utilized.

Serologic technics for the identification of unknowns are regarded in general as the most discrete and sensitive tests and may be thought of as positive in dilutions of 1:100,000.[1] It was thought that if a suitable serologic technic for the identification of Bence-Jones protein were employed a higher percentage of positive results might be recorded in tests of urine and serum.

Identification of Bence-Jones protein has been somewhat hampered by the fact that the physical, chemical and immunologic properties of this protein have never been thoroughly explored. Some workers have regarded the term as representing a collection of proteins,[2] similar in their qualities and properties, whereas others have thought that the term referred to a specific protein defined by the limits of investigative work, admittedly incomplete.[3] Unfortunately, however, the paucity of definitive knowledge in this field has not served to stay the flow of a wave of relevant positive statements, many of which are groundless.

*From the Department of Clinical Pathology of the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute. Supported by a grant from the Harkins Medical Research Foundation.

A portion of this paper was presented before the 1951 Annual Meeting of The American Society of Clinical Pathologists October 15, 1951, in Chicago, Illinois.

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In the studies to be described, the initial premise was made that the term was a loose one employed to embrace those protein or protein-like substances whose peculiar precipitative properties were defined by Henry Bence-Jones in 1847.[4] Although Bence-Jones proteinuria has been reported in many conditions, it is most commonly associated with myelomatosis.[5] The great variation in the size and the cytoplasmic and nuclear configuration of the individual plasma cells encountered in aspiration studies of myeloma marrow, with the different anatomic forms in which this disease presents itself were thought possibly to represent a reflection of biologically different diseases with equivalent variation in the Bence-Jones protein excreted. For this reason, the immunologic studies were initiated with the thought of demonstrating immunologic variation in samples of Bence-Jones protein obtained from different patients.

Albumin-free urine from patients in whom the cytologic diagnosis of myelomatosis had been established was treated with acetic acid until a pH of 5.0 was reached. This acidified urine was then saturated with sodium chloride to precipitate the Bence-Jones protein. Of the many procedures for precipitating Bence-Jones protein, this was thought to be the most benign from the standpoint of alteration of its antigenic structure. The precipitates thus formed were placed in semipermeable membranes and dialyzed against distilled water until the dialysates were demonstrated to be chloride free. These purified protein precipitates were then made up in a 20 per cent suspension and used to produce immune rabbit serums. Sufficiently high titers were obtained by four courses of five daily injections of 10 cc. of 20 per cent suspension with one week's rest period used between the courses.

Complement-fixation and precipitin tests demonstrated that, contrary to the original tenet, all the Bence-Jones proteins investigated were immunologically identical. Because of the simplicity of the test the precipitin test was adopted as standard, and 0.1 cc. of the clear supernatant fluid from the antigen with pH adjusted to 7.0 was overlaid with 0.2 cc. of the clear supernatant from centrifuged immune serums.

The demonstration of the immunologic identity of the Bence-Jones proteins investigated rendered the antiserums of value in diagnosis. High-titer immune serums were used in precipitin tests of urine samples of both undiagnosed patients and patients in whom the diagnosis of myelomatosis had been established by morphologic means. Twenty-four-hour urine specimens, demonstrated chemically to be albumin-free, were placed in semipermeable membranes and concentrated to 50 to 70 per cent of their original volume. The pH was adjusted to 7.0 after dialysis against distilled water, and a quantity was centrifuged sufficiently to render the supernatant absolutely clear. One-tenth cc. of this treated urine was overlaid with 0.2 cc. of the clear immune serum and incubated at 37° C. for one hour, after which fixation at refrigeration temperature was effected overnight. In many cases a gross precipitate at the interface was observed immediately after the urine had been overlaid with immune serum. In other instances the precipitate was observed after the refrigeration fixation. The test tubes were allowed to assume room temperature after removal from the refrigerator before the tests were interpreted. This was necessary to obviate false positive reactions due to the presence of cryoglobulins, which had previously been shown to be absent in all the test antiserums but presumably could be present in the urine. For each test two controls were employed; normal human urine, treated as described above, was overlaid with immune serum, and urine with chemically proved Bence-Jones protein was overlaid with normal rabbit serum. These controls were uniformly negative. Urine samples with chemically demonstrable Bence-Jones protein, when overlaid with immune serum, were consistently positive. Similar precipitin tests on normal human marrow were shown to be positive, with absolute correlation being found between the serologic and chemical tests for Bence-Jones protein in all the marrow serums examined.

After the demonstration of cross-precipitin reactions proving the immunologic identity of the various samples of Bence-Jones protein tested, the immune rabbit serums were utilized clinically for testing the urine specimens of patients in whom the chemical tests for Bence-Jones protein had been reported negative. Ten patients with negative chemical tests and positive precipitin tests were later shown by marrow-aspiration studies to have myelomatosis. Positive precipitin tests and negative chemical tests were reported on 3 patients in whom subsequent laparotomy disclosed solitary plasmacytomas. A positive precipitin test in the face of a negative chemical report was observed in the urine of a patient whose marrow and peripheral-blood studied demonstrated a morphologic picture of lymphatic leukemia. Positive precipitin tests were noted in 2 additional patients whose final diagnoses are still pending. On one of these patients marrow-aspiration studies were not diagnostic but disclosed an increased number of plasma cells; roentgen studies of this patient revealed a number of osteoporotic areas suggestive of multiple myeloma. Marrow-aspiration studies of the other patient, suggestive of myelomatosis, were submitted for re-evaluation to other hematologists, all of whom concurred in the compatibility of the marrow smears with the diagnosis of multiple myeloma.

These last 2 cases are the only investigations in which clinical proof of the suspected findings is not immediately evident. It is fairly apparent at this state of the investigation that they will not represent false positives.

Traditionally, the excretion of Bence-Jones protein is not supposed to be constant.[6] For this reason twenty-four-hour urine specimens were obtained and concentrated early in the project. It is our concept that after the initial appearance of the protein in the urine it is always present but perhaps in minimal concentration. The basis for the statement concerning the vacillation of its appearance appears to lie in the inability of chemical tests to demonstrate the protein in low concentrations. In the small series reported here, Bence-Jones protein could be demonstrated serologically in every urine specimen examined, regardless of how dilute or how small in quantity.

Since it is necessary to have fairly high concentration of Bence-Jones protein (0.3 gm. per 100 cc.) to detect its presence chemically, it is believed that the serologic test will offer aid in establishing the presence of this bizarre protein in the early stages of disease. The occasional appearance of this protein in the urine of patients not shown to have multiple myeloma appears to be of prognostic importance, and for that reason alone its presence should be ascertained. Admittedly, the finding of Bence-Jones protein in the urine or serum is most often associated with multiple myeloma or one of its variants. The diagnosis of multiple myeloma is often not made until late in the course of the disease, and it is thought that this test may offer the clinician a positive diagnosis at a somewhat earlier stage.

Summary

A new technic is described for the positive identification of Bence-Jones protein in low concentration. The test consists of producing immune rabbit serums against chemically proved Bence-Jones protein. These serums were initially utilized to demonstrate the immunologic identity of a number of samples of Bence-Jones protein. The serums were then employed clinically to evaluate urine specimens on which the chemical tests for Bence-Jones protein were negative. No known false positive or false negative tests have been observed. Ten patients with negative chemical tests but positive serologic tests for Bence-Jones protein in the urine were later shown by morphologic means to have multiple myeloma. Three patients with similar laboratory studies were shown by laparotomy to have so-called solitary plasmacytomas. Two additional patients had positive serologic but negative chemical tests for Bence-Jones protein. Marrow-aspiration studies of these patients were compatible with myelomatosis. Similar laboratory findings were noted in a patient with chronic lymphatic leukemia. It is suggested that this test is of value in establishing the presence of Bence-Jones protein at a relatively early stage of disease. The high correlation of Bence-Jones proteinuria with multiple myeloma indicates that the test may be of value in study of this disease in earlier phases.

References

1. Smith, D. T., and Martin, D. S. *Zinsser's Textbook of Bacteriology.* Ninth edition, 992 pp. New York: Appleton-Century-Crofts, Incorporated, 1948.
2. Wells, H. G. *The Chemical Aspects of Immunity.* 254 pp. New York: The Chemical Catalog Company, Incorporated, 1925.
3. Massini, R. Untersuchung bei einem Falle von Bence-Jones'scher Krankheit. *Deutsches Arch. f. klin. Med.* **104**:29–43, 1911.
4. Bence-Jones, H. On new substance occurring in urine of patient with mollities ossium. *Phil. Tr. Roy. Soc. London*: 55–62, 1848.
5. Geschickter, C. F., and Copeland, M. M. *Tumors of Bone.* Third edition. 810 pp. Philadelphia: J. B. Lippincott Company, 1949.
6. Lichtenstein, L., and Jaffe, H. L. Multiple myeloma: Survey based on 35 cases, 18 of which came to autopsy. *Arch. Path.* **44**:207–246, 1947.

DOCTORS AFIELD

Albert Schweitzer: Physician, Philosopher, Theologian, Musician

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MANY physicians have carved out distinguished careers in other fields than medicine after having acquired their basic medical training. It remains for a very few persons to enter medicine after major success in another profession. Yet Albert Schweitzer did this, not after success in one

activity, but after he had earned doctorates and world-wide reputations in three quite dissimilar fields — philosophy, theology and music. He began his medical studies in 1905 at the age of thirty, pursued them under conditions that would have moved most medical students to give up in despair, and went on to establish a hospital on the River Ogowe in Gabon, French Equatorial Africa, at the village of Lambaréné, which has become legendary in his lifetime.

What manner of man is this jungle physician, who finds time to become a world authority on the life of Bach as well as a superlative interpreter of his organ works, a minister who inspires Christ-like devotion, and a philosopher and ethical thinker whose message to mankind offers reason for hope in

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a world seemingly bent on its own destruction? Work is a master word to him, as to Sir William Osler, but it is only one of several. Linked with prodigious industry is a profound intelligence. Interweaving the two is the real key to the understanding of the man — namely, a very sensitive, perceptive awareness of the needs of all human beings, indeed of all things that live. His basic philosophy is that of "reverence for life," whose ethic "comprehends within itself everything that can be described as love, devotion and sympathy, whether in suffering, joy, or effort."[1] By giving thought to the meaning of life that wills to live in the midst of other, similarly aspiring life, man may become aware of the tragic paradoxes that follow from the fact that some life must be destroyed in order that other life may go on. If one becomes aware, then one may hope to develop the ability to distinguish between what is less and what is more evil. He believes that only by intensely individual thought can man become truly ethical and bring himself back from uncivilization and misery to true civilization.[2]

What makes this philosophy of his so challenging is that its application by a substantial number of the world's peoples would abolish war and ameliorate human misery almost at once, or at least reverse an apparent downward trend. It is intertwined with Schweitzer's quite literal Christianity, but harmonizes with all religions as well as with the ideals of persons who are keenly intelligent and thoughtful but cannot bring themselves to adopt a dogmatic religion.

Schweitzer is now seventy-seven years of age, and the pattern of his life can be seen virtually complete. In his childhood years most of the qualities that have made him remarkable were to some degree evident. He was so keenly aware of the poverty of those about him that he would not eat or wear what his schoolmates could not have. He could not endure the suffering of people or animals without trying to do something about it. His passion for reading was unlimited. An excellent sense of humor has always been present. Music produced in him almost unbearable pleasure, and by the age of nine he substituted for the regular church organist.

All was not smooth and serene in his childhood by any means. He had, as he says, "inherited a terribly passionate temper"[3] against which he has always had to be on guard. He was shy and reserved. To learn to read and write took much effort, and languages and mathematics were quite difficult. He was much given to day-dreaming. But, as he says, "After a time I felt a certain fascination in mastering subjects for which I had no special talent."[4]

As he grew up and mastered one field after another, he became persuaded that if he possessed any unusual abilities they must be put to work for the benefit of those less fortunate than himself. As he was pondering this problem, he made the decision, at the age of thirty, to take a medical course and go to Africa, there to minister to the people who seemed the most neglected of all human beings. The hospital that he established at Lambaréné has had many vicissitudes; it has survived the severe ravages of two world wars, and now takes care of nearly 300 patients on a budget that would excite the disbelief of any hospital administrator. He has supported the hospital by organ concerts given on his periodic trips to Europe, by lectures and by gifts from admirers in all countries. In the brief intervals between his African sojourns he makes his headquarters in the old family home at Gunsbach in Alsace.

Any busy doctor can sympathize with his plaintive comment in his journal during a particularly busy time:[6]

> There are also surgical patients whose dressing must be renewed, water must be distilled, and medicine prepared; sores must be cleansed, and there are teeth to be drawn! With this continual drive and the impatience of the waiting sick, I often get so worried and nervous that I hardly know where I am or what I am doing.

In spite of all his work all day long he has found it possible to work on his philosophy or other writings several hours each evening. He has written more than a dozen books, ranging all the way from theological treatises such as *The Quest of the Historical Jesus* and the monumental biography of Johann Sebastian Bach, to his multivolume work, not yet completed, *The Philosophy of Civilization.* An even greater number of books have been written about him. He is an authority on organs, particularly their preservation and reconstruction, and he has recorded much of Bach's organ music, the latest records being due for release in the fall of 1952.

Some of the flavor of his thought may be gained by extracts from his various works of a few of the many short, meaningful statements that are really aphorisms. Among these are: "To become ethical means to begin to think sincerely."[7] "The ethics of sincerity toward oneself passes imperceptibly into that of devotion to others."[8] "Ethics are responsibility without limit to all that lives."[9] "Anyone who proposes to do good must not expect people to roll stones out of his way, but must accept his lot calmly if they even roll a few more upon it."[10] "The good conscience is an invention of the devil."[11] "There are no heroes of action: only heroes of renunciation and suffering."[12] "I, therefore, stand and work in the world as one who aims at making men less shallow and morally better by making them think."[13] "Reverence for life contains in itself resignation, an affirmative attitude toward the world, and ethics."[14] "To the question as to whether I am an optimist or a pessimist, my answer is that my knowledge is pessimistic but my willing and hoping are optimistic."[15]

After a careful study of his life one can only conclude with Albert Einstein, "There, in this sorry world of ours, is a great man."

References

1. Schweitzer, A. *Out of My Life and Thought.* 274 pp. New York: Henry Holt & Co., 1949. P. 159.
2. *Ibid.* P. 160.
3. Schweitzer, A. *Memoirs of Childhood and Youth.* 78 pp. New York: Macmillan, 1949. P. 23.
4. *Idem.*[3] P. 4.
5. Tribute to Albert Schweitzer by Charles Munch. In Joy, C. C. *Music in the Life of Albert Schweitzer.* 300 pp. New York-Boston: Harper and Brothers-Beacon Press, 1951. (Preface.)
6. Schweitzer, A. *On the Edge of the Primeval Forest and More From the Primeval Forest.* 229 pp. New York: Macmillan, 1948. P. 57.
7. *Idem. The Philosophy of Civilization.* 347 pp. New York: Macmillan, 1949. P. 308.
8. *Ibid.* P. 314.
9. *Ibid.* P. 311.
10. Schweitzer.[3] P. 112.
11. *Idem.*[2] P. 318.
12. *Idem.*[3] P. 111.
13. *Ibid.* P. 219.
14. *Ibid.* P. 232.
15. *Ibid.* P. 279.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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CASE 38281

Presentation of Case

A forty-one-year-old man was admitted to the hospital because of dyspnea, cough and edema of the legs.

Four months before admission the patient first noted the onset of a nonproductive cough, which was associated with a feeling of general malaise, weakness and easy fatigability; on three occasions, the last one a few days prior to entry, he expectorated about half a teaspoonful of blood. There were no night sweats, pleurisy, joint pains or fever. Three months before admission he noted painless swelling of the legs, dyspnea on exertion, orthopnea and occasional paroxysmal nocturnal dyspnea. Treatment with a low-salt diet, digitalis, and frequent mercurial injections failed to relieve the symptoms. For the two months before entry he received resins in addition to the above treatment, but the symptoms continued and in addition he had occasional nausea and vomiting and some leg cramps. The resin, low-salt diet and mercurial diuretics were discontinued four days before admission, but this had no effect on his condition. He continued to work at a desk job until the day before admission.

Four years prior to entry when he consulted his physician because of night sweats and a chronic cough, he was told that he had a "tuberculous cavity" in the lung. He was kept in bed for seven weeks and then gradually resumed normal activity; he had felt quite well in the interval until the onset of the present illness. He had had a bilateral inguinal herniorrhaphy twenty years and an appendectomy nine years before entry.

Physical examination revealed a well nourished man in no acute distress while lying flat. There was a slight cyanotic tinge to the lips. The neck veins were distended to the angle of the jaw in the upright position. The chest was increased in the anteroposterior diameter; it was clear throughout. The heart was moderately enlarged to the left. The rhythm was regular, and the pulmonic second sound was louder than the aortic. There was a harsh Grade II to III systolic murmur in the aortic area, transmitted to the neck, apex and left axilla; on repeated examinations it was noted to be loudest at the third and fourth interspaces near the left sternal border. The abdomen was obese and protuberant, and a slightly tender liver was palpated 2 cm. below the costal margin. There was a large reducible left inguinal hernia. Severe edema of the upper and lower legs was present, slightly more marked on the left.

The temperature was 99°F., the pulse 110, and the respirations 25. The blood pressure was 140 systolic, 90 diastolic.

The urine had a specific gravity of 1.020 and gave a ++ reaction for albumin; the sediment contained 10 white cells and a few hyaline and cellular casts per high-power field. Examination of the blood revealed a hemoglobin of 12.2 gm. and a white-cell count of 11,100. The serum sodium was 130.0 milliequiv., the chloride 96 milliequiv., the carbon dioxide 28.5 milliequiv., and the potassium 4.1 milliequiv. per liter; the nonprotein nitrogen was 38 mg., the total protein 6.43 gm. per 100 cc., with an albumin-globulin ratio of 1.2, and the serum bilirubin 0.8 mg. direct and 1.2 mg. total per 100 cc. The pH of the blood was 7.46. A blood Hinton test was negative. The sputum was negative for acid-fast organisms. The vital capacity was 1.4 liters, or 34 per cent of normal. The venous pressure was equivalent to 300 mm. of water. Roentgenograms of the chest revealed a coarse strand-like increase in density in the left upper lobe, which appeared to be slightly reduced in size; the lungs were

otherwise clear (Fig. 1). Diaphragmatic motion was free and equal. The heart was prominent in the region of the left ventricle. There was a small hiatus hernia. An electrocardiogram revealed normal sinus rhythm at a rate of 90, with right-axis deviation. The PR interval was 0.16 second, and the QRS interval 0.09 second; the T waves were low and upright in Lead 1, flat in Lead AVL and diphasic in Leads 2, 3 and AVF. The Q waves were present in Lead 3; the QR waves were present in Lead AVR, and V_1, progressing to small R and S waves of equal size in Lead V_6. The P waves were prominent in all precordial leads. Cardiac-catheterization studies revealed a volume of 12 liters per minute, an oxygen consumption of 270 cc. per minute, arterial oxygen saturation of 92 per cent and a cardiac index of 2.18 liters per minute per square meter. The pulmonary arteriolar resistance was 1850 dynes per second per cm.$^{-5}$ per square meter. The pressure in the right pulmonary artery was equivalent to 117 to 138 mm. of mercury systolic and 38 mm. diastolic. The pressure in the right ventricle was 100 to 116 mm. of mercury systolic and the end diastolic pressure was equivalent to 20 mm. of mercury. The mean pulmonary "capillary" pressure was equivalent to 15 mm., and the mean pressure in the right auricle to 18 mm. of mercury.

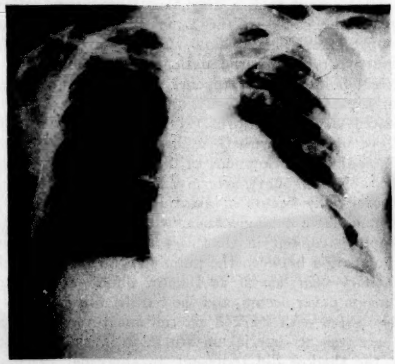

FIGURE 1.

He improved somewhat in the hospital and was discharged on the eleventh day to continue with the low-salt diet, digitalis and mercurial diuretics.

The patient allegedly improved on this regimen sufficiently to return to work and to drive the family car for several hours at a time. One afternoon three months after discharge he suddenly became severely cyanotic and breathless; the symptoms grew progressively severe, and he was dead within a few minutes of arrival at the hospital.

DIFFERENTIAL DIAGNOSIS

DR. PAUL DAVISON*: The history is one of the insidious onset of failure of the right side of the heart in a man of early middle age, terminating within nine months of the onset of symptoms. The nausea, vomiting and cramps that the patient suffered in the few weeks prior to admission to the hospital were probably due to the syndrome of sodium depletion, which was induced by the rather drastic but unsuccessful attempts to eliminate the edema. This view is supported by the electrolyte studies on admission, which showed the serum sodium reduced to 130 milliequiv. per liter. The other biochemical data and the urinary findings are consistent with a failing heart. The repeated hemoptyses, the noted accentuation of the pulmonary second sound and the electrocardiographic evidence of right ventricular hypertrophy all indicate that the patient had probably had long-standing pulmonary arterial hypertension. This is confirmed by the catheter studies; the resting cardiac output was somewhat diminished — the cardiac index was 2.18 liters per minute per square meter, the normal being about 3.3 liters; the pulmonary-artery pressure was greatly elevated (about four or five times the normal, the mean value of which I calculated to be approximately 65 mm. of mercury) because of a marked increase in the pulmonary arteriolar resistance; 1850 dynes per second per cm.$^{-5}$, per square meter, compared to a normal value of 250 to 300 dynes; or about sixfold of normal. The end ventricular diastolic pressure of 20 mm. of mercury and the right auricular mean pressure of 18 mm. of mercury confirmed the presence of right ventricular failure.

On these findings I can exclude a number of possible causes of the syndrome of right-sided heart failure, such as constrictive pericarditis, congenital pulmonary valvular stenosis and obstruction of the main pulmonary artery by either clot or aneurysm. Among the possible causes of increased pulmonary arterial resistance, which eventually leads to right-sided heart failure, I must consider that of parenchymatous pulmonary disease. The patient gave no evidence of a chronic chest disease. Clinically, the lung fields were clear, and radiologically, apart from the shadow at the left apex, they were also clear. The arterial oxygen saturation was 92 per cent; carbon dioxide retention was not demonstrated, and the blood pH was on the alkaline side of normal. All these factors are strongly against a diagnosis of any chronic parenchymatous disease. Moreover, in such conditions pulmonary hyper-

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tension of this degree is rare, and when it does occur with right-sided heart failure, it is invariably accompanied by a reduction in arterial oxygen saturation.

The possibility of a mitral stenosis arises in any case that presents marked pulmonary hypertension, and sometimes in such cases the increased pulmonary arteriolar resistance may mask the clinical picture; in spite of that, however, one can always find evidence of mitral stenosis, and in this patient there was no clinical or radiologic evidence of mitral stenosis. Admittedly, the pulmonary capillary pressure of 15 mm. of mercury was slightly above normal, but since it is difficult to measure in cases of this type, I think I shall disregard it. I do not think this patient had mitral stenosis.

The cause of the increased pulmonary arteriolar resistance must have been some vascular abnormality of the pulmonary bed either from recurrent pulmonary emboli that had gradually occluded the vasculature or from some intrinsic disease of the pulmonary vascular bed, or a condition secondary to some congenital cardiac defect. I think it is highly improbable that it was a case of progressive occlusion of the pulmonary vascular bed by peripheral emboli. The cough and slight hemoptysis can be attributed to the severe degree of pulmonary hypertension. The patient had no history of peripheral phlebothrombosis and no previous history of pulmonary infarction.

The possibility of an intrinsic pulmonary vascular abnormality, so-called primary pulmonary hypertension, I shall leave to the last because it is a diagnosis that one is forced to make in the absence of any other demonstrable cause.

The congenital cardiac abnormalities that can produce pulmonary hypertension and right-sided heart failure are atrial septal defect, ventricular septal defect, Eisenmenger's syndrome and abnormal communications between the pulmonary artery and the aorta, such as patent ductus and aortic septal defect. The radiologic configuration of the heart is very much against an atrial septal defect. In such a condition the pulmonary arteries in the hilus are very widely dilated. The majority of such cases give evidence of partial right-bundle-branch block, and there was none in this case. The mean right auricular pressure was 18 mm. of mercury and it certainly must have exceeded that in the left auricle; therefore, if there was a wide atrial septal defect, the shunt would have been reversed, with evidence of arterial unsaturation. With regard to ventricular septal defect and Eisenmenger's syndrome associated with pulmonary hypertension, all such patients, when they eventually show heart failure, have a considerable degree of arterial unsaturation as the result of the reversed shunt. I think that on these grounds I can exclude them.

Lastly, I am left with a patent ductus arteriosus or aortic septal defect. In such instances the characteristic murmur may disappear, the diastolic element may disappear, and the patient may present a clinical picture very similar to this if during rest the pulmonary and aortic pressures are so evenly balanced that there is no significant shunt either from right to left or from left to right. There was no direct evidence of that. The catheter was not passed through a "patent ductus" or aortic septal defect. It is a possibility that should be considered. Certainly the form of death with the sudden onset of severe cyanosis suggests a final occlusion of the pulmonary vascular bed incompatible with life, with a terminal reversal of the shunt from the pulmonary artery to the aorta.

If I accept such a diagnosis, I am forced to explain the cause of the x-ray shadow in the left upper lobe. This shadow was presumably present four years before the patient was admitted with heart failure, and it appears to have been vascular in origin. Such a picture is unlikely in a patient with patent ductus arteriosus. If it was vascular it would have been more likely to have been due to some anomalous development of the pulmonary vascular bed. A pulmonary arteriovenous aneurysm, which occasionally occurs in association with hereditary hemorrhagic telangiectasia, will produce such an appearance, but in that case there is a free communication between the pulmonary artery and pulmonary vein; as far as I know pulmonary hypertension never occurs, and the condition is invariably associated with marked arterial unsaturation. Since there was no arterial unsaturation in this patient, if the shadow did represent an abnormal vascular communication it could not have been a pulmonary arteriovenous aneurysm. There is, however, a very rare form of pulmonary vascular abnormality that has to be considered — that is, an abnormal communication between bronchial arteries or anomalous systemic arteries and the pulmonary bed, often with the pulmonary arteries themselves. These cases may show a picture of pulmonary hypertension. I believe that it is conceivable that that shadow in the left upper lobe was vascular, and represented an anomalous communication between the bronchial and the pulmonary artery acting as a diffuse "patent ductus" that was responsible for the secondary pulmonary hypertension, the right-sided heart failure and death.

The final diagnosis that I must make is idiopathic primary pulmonary hypertension, but I believe that the diagnosis of anomalous bronchial arteries entering the pulmonary vascular bed is a possible one.

I should like to hear the opinion of the radiologist.

DR. JAMES J. MCCORT: The change in the left upper lobe was thought not to be due to tuberculosis of four years' duration because of the absence of fibrosis, calcification or cavitation. We did wonder about anomalous dilated vessels in the left upper lobe, but it seems more likely that

these prominent vessels are branches of the pulmonary artery; I do not think I can go any farther than to say a vascular anomaly is a possibility. The heart is increased in size and shows the appearance of cor pulmonale, with very marked enlargement of the right ventricle anteriorly; the undivided portion of the pulmonary artery is also dilated, but the larger branches of the pulmonary artery with the exception of those to the left upper lobe are not dilated (Fig. 1).

Dr. Paul D. White: I would like to ask if pulmonary endarteritis obliterans might be the answer?

Dr. Davison: When I said that the diagnosis was primary idiopathic pulmonary hypertension, I implied that, but if one accepts that diagnosis one cannot explain the marked vascular pattern at the left apex.

Dr. Howard B. Sprague: We made a tentative diagnosis of cor pulmonale, and went ahead with the catheter studies only in the hope that they might give evidence of constrictive pericarditis or some condition that we could do something about. But when Dr. Myers completed the studies, we were left again with the diagnosis of cor pulmonale, which we believed was due to some vascular obstruction in the lungs and not secondary to either valvular disease or a congenital defect.

Dr. White: Do you think it was an arterial rather than a venous shadow?

Dr. McCort: Yes; the vessels seem to come off the left pulmonary artery.

Clinical Diagnoses

Chronic cor pulmonale.
Pulmonary fibrosis.

Dr. Davison's Diagnosis

Primary idiopathic pulmonary hypertension.

Anatomical Diagnoses

Chronic multiple pulmonary embolization with recanalization.
Cor pulmonale.
Thrombophlebitis, old, left common femoral vein.

Pathological Discussion

Dr. Benjamin Castleman: The heart weighed about 480 gm. and demonstrated predominantly right-sided hypertrophy; the right side measured 9 mm., about three times the normal thickness, and the left measured 10 mm., almost the same size. On opening the pulmonary artery to the left lower lobe, we found a large occluding thrombus; that to the right was free from old thrombi but did contain fresh emboli. These occlusions certainly accounted for the sudden death in this patient. The left upper pulmonary artery was dilated and apparently accounted for the x-ray shadow.

Of course, one cannot explain the marked hypertrophy of the right side of the heart and cor pulmonale by occlusion of only one lobe so we predicted that we would find other evidence of occlusion in the pulmonary arterial tree. The microscopical sections of both lungs showed blocked arterioles in all the lobes. In these blocked pulmonary arterioles were channels of recanalization, in some of which new endothelium had already been formed (Fig. 2 and 3). Dr. White may prefer to call this endarteritis obliterans; I am reluctant to make that diagnosis because I believe that most of these cases are due to emboli. In this case we found the source for the multiple embolization that he had probably been having for years — an old thrombophlebitis of the left common femoral vein that was almost

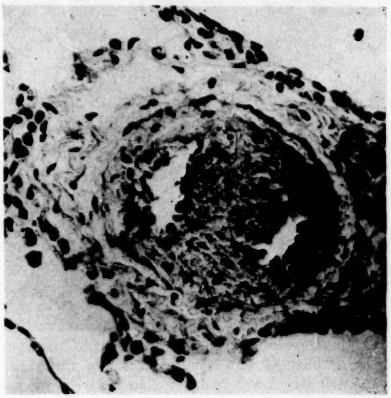

Figure 2.

occluded. Dr. Bland and I[1] reported a similar case some years ago; in that case we believed the embolization had occurred at least nine years before death from cor pulmonale.

Dr. White: Did the walls of the smaller pulmonary vessels look reasonably normal?

Dr. Castleman: There was no evidence of previous arteritis. It is interesting that in the walls of the larger bronchi, the bronchial arteries were very much thicker than normal. Unfortunately, the main bronchial artery was not found because the lungs were not injected before sectioning. When this sort of process organizes further it may simulate arteriosclerosis of the pulmonary artery. Harrison[2,3] has shown conclusively that emboli introduced into the jugular veins of animals can produce, after lodging in the pulmonary arteries and organizing, a picture indistinguishable from arteriosclerosis.

Dr. Walter Bauer: What did he inject?

DR. CASTLEMAN: Fibrin clots. In the end stage the picture is that of intimal hyperplasia, which in the old days was called Ayerza's disease. Dr. Bland and I have several such cases most of which had been called Ayerza's disease but which are really due to emboli, not thrombi or endarteritis. In their experimental work Muirhead,[4] in Texas, and Wartman,[5, 6] in Chicago, have also shown that emboli

FIGURE 3.

can produce the picture of arteriosclerosis in the pulmonary vessels.

DR. WHITE: This case emphasizes the need of everlastingly looking for trouble in the leg veins.

DR. SPRAGUE: Was this characterized by the finding that you and Dr. Bland reported — namely, that the emboli seemed to be all the same size, and lodged in vessels of the tertiary radicles?

DR. CASTLEMAN: By and large that was true; the one in the left pulmonary artery was large and very adherent; in the other four lobes, the emboli were all small.

DR. WHITE: Do you visualize this as fragmentation of an embolus after it reaches the pulmonary artery or as many minute emboli?

DR. CASTLEMAN: I should prefer the latter.

DR. GORDON S. MYERS: Were there infarcts in the left lower lobe?

DR. CASTLEMAN: No.

DR. WHITE: This case helps to clear up Ayerza's disease.

REFERENCES

1. Castleman, B., and Bland, E. F. Organized emboli of tertiary pulmonary arteries. *Arch. Path.* **42**:581-589, 1946.
2. Harrison, C. V. Experimental pulmonary arteriosclerosis. *J. Path. & Bact.* **60**:289-293, 1948.
3. *Idem.* Experimental pulmonary hypertension. *J. Path. & Bact.* **63**:195-200, 1951.
4. Muirhead, E. E., and Montgomery, P. O'B. Thromboembolic pulmonary arteritis and vascular sclerosis. *Arch. Path.* **52**:505-517, 1951.
5. Wartman, W. B., Jennings, R. B., and Hudson, B. Experimental arterial disease. I. Reaction of pulmonary artery to minute emboli of blood clot. *Circulation* **4**:747-755, 1951.
6. Wartman, W. B., Hudson, B., and Jennings, R. B. Experimental arterial disease. II. Reaction of pulmonary artery to emboli of filter paper fibers. *Circulation* **4**:756-763, 1951.

CASE 38282

PRESENTATION OF CASE

A fifty-nine-year-old man entered the hospital because of unremitting fever.

The patient, who had been well, about five weeks before admission after a bout of sneezing, developed a sharp, steady ache in the right sacroiliac region. Shortly after this he developed pain in the lower lumbar region and three or four days later in the right lower chest; the pain was aggravated by motion, but was not severe enough to limit his activity. These pains gradually subsided, disappearing entirely after about two weeks. Three weeks before entry he developed a sharp, steady, severe pain in the left precordium that was aggravated by deep breathing or coughing. In addition he began to have repeated bouts of fever, with a maximum temperature of 103°F., followed by slight chills and sweating; these bouts occurred four or five times a day and left him tired and covered with perspiration. He also had a slight dry cough, and gradually increasing anorexia and malaise. His physician treated him for eighteen days, without effect, with penicillin, aureomycin and a sulfonamide. Four days before admission, he was seen by another physician, and again treatment with penicillin, chloromycetin and terramycin had no effect, chest pain, chills, fever, profuse sweating and a mild cough productive of small amounts of yellow sputum continuing.

There had been marked anorexia and a loss of 20 to 30 pounds in weight since the onset. For a few weeks before admission his voice had been hoarse. There had been no nausea, vomiting, diarrhea, dyspnea, orthopnea, hemoptysis, jaundice, ankle edema, skin lesions, arthritis or past history of serious illnesses. For the twenty-five years prior to entry he had worked as a car painter using lacquers and enamels. He was born in Lithuania and had come to this country at twenty-eight years of age.

Physical examination revealed a co-operative man lying flat in bed in no distress. There was slight muscular weakness of the laryngeal muscles but no other abnormality of the mouth, nose or throat. The neck veins were flat. The chest was slightly emphysematous. It showed normal respiratory excursions and was resonant throughout; there were a few moist rales at the left base. The heart sounds

were normal, and no murmurs were present. There was no peripheral edema. Abdominal, neurologic and rectal examinations were negative.

The temperature was 102.4°F., the pulse 80, and the respirations 20. The blood pressure was 140 systolic, 80 diastolic.

The urine had a specific gravity of 1.017 and gave a + reaction for albumin; the sediment contained 0 to 1 red cells and an occasional hyaline cast per high-power field. Examination of the blood showed a hemoglobin of 11.2 gm. per 100 cc. and a white-cell count of 16,900, with 39 per cent neutrophils, 30 per cent lymphocytes, 18 per cent atypical lymphocytes, 7 per cent band forms, 4 per cent monocytes and 2 per cent eosinophils. The serum sodium was 130 milliequiv., the chloride 96 milliequiv., and the potassium 4.5 milliequiv. per liter; the serum calcium was 9.3 mg., the phosphorus 4.3 mg., the alkaline phosphatase 8.7 units, the fasting blood sugar 121 mg., the nonprotein nitrogen 48 mg., the total protein 10.7 gm., the albumin 1.85 gm., and the globulin 8.85 gm. per 100 cc. A bromsulfalein test showed 19 per cent retention of the dye, cephalin flocculation was + in twenty-four and forty-eight hours, and the prothrombin time was 16 seconds (normal, 13 seconds). Numerous blood cultures showed no growth. Agglutinins for brucella, typhoid and Proteus Ox-19 and Ox-2 were negative in all dilutions; those for Proteus Ox-K were positive in dilution 1:20, 1:40 and 1:80 and negative in dilution 1:160. A roentgenogram of the chest showed a prominent left ventricle, a tortuous aorta and prominence of the hilar pulmonary vascular shadows; the liver and spleen were of normal size. Films of the pelvis, ribs, skull and upper femurs were not remarkable. An electrocardiogram revealed a normal record. Lumbar puncture demonstrated clear spinal fluid and normal dynamics, cytology and chemistry; culture of the spinal fluid produced no growth. Aspiration smears of the bone marrow of the iliac crest, rib and sternum all showed essentially the same range of cellular distribution: myeloid cells, 52 per cent; normoblasts, 14 per cent; lymphocytes, 14 per cent; large mononuclear cells, probably monocytes, 13 per cent; and 7 per cent cells that were difficult to classify but were most probably either plasma cells or reticulum cells. The maturation in the myeloid series appeared to be normal, and megakaryocytes were present.

The patient's temperature remained between 100 and 101°F., and the physical signs remained unchanged except that marked tenderness was noted over the upper ribs anteriorly. He gradually became stuporous and developed tremors and irregular cogwheel-type movements of the hands and fingers on sustained posture; neurologic examination was not remarkable. On the sixth day the serum calcium, phosphorus and phosphatase were as before, the urine gave a negative reaction for albumin (nitric acid ring test). Examination of a blood smear showed normal red cells and platelets, with 1 per cent neutrophilic myelocytes, 7 per cent band forms, 52 per cent segmented cells, 12 per cent lymphocytes, 27 per cent cells probably monocytes and 1 per cent blast forms; the hemoglobin was 10 gm. per 100 cc., and the white-cell count 16,200. His course continued steadily downhill, with deepening coma and the temperature rising to 104°F. terminally. He died on the ninth day.

Differential Diagnosis

Dr. William H. Baker*: I wonder if I may see the x-ray films?

Dr. Joseph Hanelin: I have nothing to add to the findings in the films as noted in the protocol. The bones appear normal; the skull is not remarkable. The heart is somewhat enlarged in the region of the left ventricle, and vascular markings are slightly prominent. No obvious parenchymal lesion is evident.

Dr. Baker: Were there any films of the spine?

Dr. Hanelin: No.

Dr. Baker: What about the humeri?

Dr. Hanelin: What I see of them appears normal.

Dr. Baker: In summary, this patient had a six-week course of what I interpret to have been bone pain, weight loss, anorexia, malaise, fever, anemia, marked hyperproteinemia and marked hyperglobulinemia. On the basis of this rapid fulminating course and the hyperproteinemia, I have but one recourse — to make a diagnosis of multiple myeloma.

Unremitting fever has not been noted to be a prominent characteristic of multiple myeloma but in a recent article Adams et al.[1] showed that 52 per cent of their patients had fever. In the older German literature there have been cases of multiple myeloma of a fulminating character associated with a high degree of fever. The type of fever, with bouts of temperature up to 103°F. associated with marked sweating, is commonly associated with Hodgkin's disease, carcinomatosis, miliary tuberculosis and other diseases that had been looked for by serologic tests in this case.

The bone pain was consistent with a lesion involving the bones diffusely. That it was first experienced after a bout of sneezing is characteristic of destructive lesions of bone due either to a malignant lesion or to some other process. The transitory nature of the bone pain is characteristic of multiple myeloma. He experienced pain in at least two sites in the ribs. I do not know whether a friction rub was heard at the time he had the pain in the left precordium but I assume it was not.

The fact that the patient was treated by numerous antibiotics is interesting. In the past year there have been 2 cases of patients who received large amounts of sulfonamide and thereupon developed

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a plasmacytosis of the bone marrow and of the liver, and interstitial nephritis following the sulfonamide therapy.[2, 3] Both patients also had hyperglobulinemia. Although I do not think the sulfonamides had anything to do with this patient's course it is interesting to speculate about a possible relation.

The weight loss is consistent with a diffuse process, especially a diffuse process of neoplastic cells.

The patient was a car painter who used lacquers and enamels. It is well known that benzol (benzene) will produce lymphoma in animals, but there is no clear-cut relation in the production of human tumors. Benzol was probably used in the past, but my chemist friends tell me benzol is not used in car paint now.

The patient was born in Lithuania, so the Service thought of Brill's disease or typhus occurring as a recrudescence in an immigrant to this country. That was ruled out by the negative Proteus agglutinations for OX-19 and OX-2, which should have been positive if the patient had Brill's disease.

I am at a loss to explain the hoarseness and the weakness of the laryngeal muscles. It is true that extravisceral myelomatosis most commonly involves the upper respiratory tract, and it is possible that this man had myelomatous involvement of either the vocal cord or the laryngeal muscles. Another possibility, if the diagnosis is correct, is amyloid infiltration of the laryngeal muscles. In myeloma the amyloid depositions characteristically involve rather unusual sites. Indeed Lichtenstein and Jaffe[4] say that whenever amyloid is found in rather unusual sites, the possibility of myeloma should be seriously considered.

Regarding the negative mouth, nose and throat examination, in their recent article, Adams et al.[1] pointed out that 98 per cent of their 61 patients had either an extremely carious condition of the teeth or complete edentia. Since all these patients are in the older age group, I am not sure it means much.

Next, I should like to comment on the laboratory data. The slight azotemia that this patient had is probably quite consistent with involvement of the kidneys. The fact that the blood pressure was not elevated is quite characteristic; myeloma kidneys produce uremia but usually no elevation in the blood pressure. The anemia is quite consistent with any neoplastic disease, with miliary tuberculosis and with any of the other conditions that may produce a hyperglobulinemia. The elevated white-cell count is usually found with multiple myeloma. The differential counts on the blood I am at a loss to interpret. I assume the 18 per cent atypical lymphocytes found on admission and the 27 per cent cells called "probable monocytes" noted on the sixth hospital day were probably myeloma cells. There was no mention of rouleaux formation; it occurs in about two thirds of the patients with myeloma and may be of some help in establishing a diagnosis. The low serum sodium I interpret as the result of the diaphoresis associated with the fever and poor nutritional state of the patient. The serum potassium and calcium were normal. The calcium is supposed to be elevated in the majority of cases of multiple myeloma, but in perusing the literature I found no evidence of correlation of the serum calcium values with the degree of hyperproteinemia. The phosphorus was normal. In the early literature an elevated alkaline phosphatase has not been alluded to, but in a recent series[1] 48 per cent of patients with multiple myeloma had an elevated alkaline phosphatase. The reason for this is not known. The bone lesions in multiple myeloma are osteolytic, usually without evidence of bone proliferation so that the cause of the elevated alkaline phosphatase remains obscure. The total protein of 10.7 gm., with such a high globulin fraction associated with the other symptoms, means to me that the patient had myeloma.

The bone marrow was abnormal in that there was an increase in the number of plasma cells. The normal range of plasma cells varies from author to author, but most physicians are in agreement that plasma cells should not exceed 2 per cent; certainly, the figure of 7 per cent of these cells that were interpreted as possible plasma cells is definitely abnormal. I suppose if myeloma was the diagnosis the cells that were interpreted as monocytes were probably the so-called myeloma cells — the cells that we call proplasmacytes but Wintrobe and other hematologists call myeloma cells. They are large cells with no nucleoli and do resemble monocytes.

Regarding the absence of proteinuria, it is generally recorded in the literature that the higher the protein in the serum, the less likely is Bence-Jones protein in the urine. We do not fully agree with that because in the patients we have studied over the past year who have not had Bence-Jones protein demonstrated by laboratory tests, we have been able to demonstrate Bence-Jones protein by using

Dr. Jacobson's technic. I think the great variance of the percentage of patients with myeloma who have or have not Bence-Jones protein is correlated directly with the industry of the persons assigned to look for the Bence-Jones protein. I do not say that Bence-Jones protein occurs in all patients, but I do think it will be found in a high percentage of patients if adequately looked for. It has been postulated that Bence-Jones protein does not occur in patients with hyperproteinemia because it is a protein of a low molecular weight, between 25,000 and 30,000, and forms a complex with the abnormal proteins in the circulating blood; thus, it is unable to pass through the glomeruli. Whether or not that condition existed here, I do not know. Albumin was demonstrated originally, but later the urine was negative by the nitric acid ring test. If this test is done in a careful manner with a wine glass and filter paper it is an accurate test. The nitric acid should be poured into the wine glass; the urine is poured through the filter paper, whose tip must be touching the nitric acid, and then a good interphase is demonstrated. No good interphase is demonstrated when nitric acid and urine are poured into a glass together in the usual method.

Other conditions that could cause these symptoms with hyperglobulinemia are as follows: lymphopathia venereum, which I will not even discuss; sarcoidosis, but if it had been present, I should have expected to see lesions in the chest film; cirrhosis of the liver, for which the only evidence was a slight retention of bromsulfalein; kala-azar, for which there was no evidence; and disseminated lupus erythematosus, which is a possibility. A severe anemia associated with a diffuse symptomatology could be due to disseminated lupus erythematosus. No lupus erythematosus cells were demonstrated, and none were shown in the marrow. The absence of leukopenia and the sex of this patient tend to rule out disseminated lupus erythematosus. Subacute bacterial endocarditis is another offender in causing a rise in globulin. No blood cultures were taken, and there were no cardiac murmurs and no evidence of thromboembolic phenomena; therefore, I am unable to make that diagnosis. Tuberculosis is a distinct possibility, the usual type of tuberculosis that produces a high globulin being tuberculous lymphadenitis; in the series of 65 patients with miliary tuberculosis at the Boston City Hospital reported by Chapman and Whorton[5] no mention is made of an elevated globulin. Miliary tuberculosis is a hard diagnosis to make clinically; the diagnosis in 75 per cent of the patients at the Boston City Hospital was missed prior to autopsy.

The terminal course is interesting in that the patient went into coma. I think in the small series of patients that we have treated with steroids, 3 went into coma terminally, and all 3 showed no evidence of cerebral damage to account for the coma. Coma in myeloma is a very interesting situation. It can be caused by three conditions: either an extradural tumor or dural infiltration, hemorrhage, or no demonstrable abnormality. Dr. Raymond D. Adams says he has never seen a case in which myeloma involved the brain itself. My final diagnosis is multiple myeloma probably involving the ribs, pelvis and liver, possibly myeloma kidney and questionable amyloid disease of the larynx or plasma-cell infiltration or both.

Dr. Thomas Paine: Every once in a while a patient with myeloma ends up with a fungous infection. Have you experienced that yourself?

Dr. Baker: One of the patients I have seen had lymphatic leukemia with torula present in the spinal fluid, without meningitis, and in the urine and in the blood. We have had 2 other cases of torula in the spinal fluid associated with Hodgkin's disease.

Dr. Alfred Kranes: I was visiting on the Service when this patient was on the wards. The prominent feature on admission was lethargy or stupor of a degree not adequately brought out in the protocol. During the nine days on the ward he was quite stuporous; the last three or four days he was completely comatose, and that was the reason for the lumbar puncture that many of you may have been wondering about. The history of fever and pain were of longer duration than was brought out in the record. This was essentially a problem of long-standing obscure fever. It was our opinion after following the patient for a day or two that the most likely diagnosis was some form of malignant lesion, because most fevers that go on for some time and do not respond to adequate doses of antibiotics turn out to be due to a malignant process. Although there are many exceptions, that is a good rough rule. We asked Dr. Jacobson several times to identify the obscure cells, hoping he would tell us they were plasma cells, but he was never very co-operative. We also did numerous bone-marrow aspirations. We were very puzzled. When the result of the serum protein determination was reported two or three days before death, the diagnosis seemed

much clearer to us, although even then a number of people were unwilling to accept the diagnosis of multiple myeloma.

DR. BERNARD M. JACOBSON: I want to agree with Dr. Kranes, but I was not as impressed with the diagnostic significance of the high globulin as he was. To me, in a patient with fever of unknown origin, with reticulum cells in the peripheral blood and the peculiar cells in the marrow that I could not recognize as being diagnostic of myeloma, the course and history were consistent with the diagnosis of lymphomatous involvement of the bone marrow. We know that plasmacytosis of the marrow occurs in some cases of reticulum-cell sarcoma and rarely in some chronic infections. We have never seen among our 100 cases of myeloma a phosphatase this high; the highest was 6.5 units. There are some cases of lymphoma with high serum globulin.

DR. BAKER: Were any of this group patients who received cortisone? In 2 of our 6 cases an elevated alkaline phosphatase was present during steroid therapy.

DR. BENJAMIN CASTLEMAN: Does the use of steroids raise the alkaline phosphatase?

DR. BAKER: I would not say it was due to steroids. We have depressed the alkaline phosphatase in Paget's disease by the administration of cortisone.

In the cases that Adams reported 48 per cent had an elevated alkaline phosphatase.

DR. KRANES: I do not recall a single case of multiple myeloma in which there was a high phosphatase. For a while we used that as a differential point.

CLINICAL DIAGNOSIS

Multiple myeloma.

DR. BAKER'S DIAGNOSIS

Multiple myeloma.

ANATOMICAL DIAGNOSIS

Multiple myeloma.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The only positive finding at autopsy was in the bone marrow, which showed a diffuse infiltration with plasma cells. There were no localized osteolytic lesions — the more common type of myeloma — but uniform diffuse involvement — the rarer form. This type is often difficult to detect roentgenologically, since there is no contrast. On the other hand, it should be easy to detect from a bone-marrow aspiration or biopsy. There was a good deal of pulmonary edema. The kidneys did not show any of the myeloma casts, and there was no evidence of amyloid anywhere.

DR. KRANES: The reason for his stupor was always obscure, even after we strongly suspected that the patient had myeloma. We were asked to explain why he was so stuporous and why he was twitching.

DR. CASTLEMAN: We have not found anything grossly in the brain, and the microscopical sections of the brain are not through yet. There was no evidence of extraosseous myelomatous infiltration of the dura.

REFERENCES

1. Adams, W. S., Alling, E. L., and Lawrence, J. S. Multiple myeloma. *Am. J. Med.* 6:141-161, 1949.
2. Robertson, T. Plasmacytosis and hyperglobulinemia as manifestations of hypersensitivity. *Am. J. Med.* 9:315-329, 1950.
3. Carter, J. R. Plasma cell hyperplasia and hyperglobulinemia in trichinosis. *Am. J. Path.* 25:309-312, 1949.
4. Lichtenstein, L., and Jaffe, H. L. Multiple myeloma. *Arch. Path.* 44: 207-246, 1947.
5. Chapman, C. B., and Whorton, C. M. Acute generalized miliary tuberculosis in adults. *New Eng. J. Med.* 235:239-248, 1946.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
and
THE NEW HAMPSHIRE MEDICAL SOCIETY
OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND PUBLISHED WEEKLY UNDER THE JURISDICTION OF THE COMMITTEE ON PUBLICATIONS

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MICROFILM volumes available to regular subscribers through University Microfilms, 313 N. First Street, Ann Arbor, Michigan.

MATERIAL, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

THE SHORTEST DISTANCE

IT sometimes seems that all scientific endeavor must pass through two great phases in its development. Each new discovery of apparent merit is followed by investigations that add to the complexity of an already difficult subject. This complexity increases until it appears to be almost impossible for the mind of man to grasp its myriad ramifications. Fortunately, there then comes the phase of simplification, for the impact of sufficient thought on any problem is measured in direct proportion by the degree of simplicity attained. It again becomes apparent that a straight line is the shortest distance between two points.

Great men are usually direct, sincere men, and great physicians are those who can reduce medical science to simple and direct means of aiding their patients. It is too seldom affirmed that the simple diagnosis is usually the right one and that the simple treatment is usually the most effective, and simple human understanding of another human being ranks with all the drugs and surgery that are available to medical science.

No physician can afford to be without extensive scientific knowledge and skill, but many physicians who lay their wreaths on the pedestal of pure science are surprised to find, sooner or later, that their idol is a false one. The patient comes to his physician to be comforted, and the scientific treatment of disease is but one phase of that comfort. The true physician will ease his patient's pain, give sympathetic understanding to his emotional turmoil, and classify and treat his disease with as simple and direct means as may exist.

The young physician seems too often to choose the difficult approach and is too frequently found on the path of needless complexity. The experienced practitioner seeks to simplify his problems.

It seems that many physicians are educated beyond their understanding. In the search for scientific detail and in the arduous climb to outstrip their fellows in research contributions they may forget that the great and good human values of medicine lie in the application of its genuine simplicity.

The physician whose factual knowledge outstrips his ability to understand the true values of such knowledge need not be blamed. From his earliest premedical education until he reaches a post of responsibility in the profession, he has seen emphasis placed on science almost to the exclusion of the true value of the physician in practice, which is, and always will be, his value to his patients. Young men who are being trained in medicine should be taught to avoid the difficult problems until they not only know but understand the simple ones. They should be taught again and again that their true value to their own patients, and to their own students as time goes on, will be measured in their ability to try to understand a human being and to attack his problems whether or not they are those of disease. They should be taught that the true phy-

sician has achieved his success by reducing the complexities of medicine to simple means of treating human beings.

In the education of the doctor the value of simple therapy should be emphasized. Many splendid and time-tried therapeutic aids are forgotten in the scramble for new and more effective forms of treatment. Specific remedies are considered, but little is said about auxiliary measures for relief. Few students, even in their senior year, know anything beyond the term itself of rest — the greatest single therapeutic agent at our command.

Most young physicians, when they begin practice, have a brain full of knowledge that may be quite correct, but most of which is complicated beyond any hope of applicability. This complexity is neither necessary nor desirable. Rather, let the young man know the basic principles of disease with which he must struggle, and know them well; let him know the value (or lack of it) of the simple, basic procedures of diagnosis and therapy. And, most important, let him know the true value of the physician himself, which, whether we of the profession approve it or not, is measured in terms of humility, simplicity and understanding of human beings.

When such an ideal comes to be the goal of the profession there will be more great physicians and no fewer great scientists.

TRAVELERS AID

Now that the Fourth of July cannon cracker has been relegated to the limbo of the past and the householder's mind is at rest so far as any danger from high explosives is concerned — the atomic threat being an apparently accepted accompaniment of daily life — he can give full attention to his summer week-end and vacation hazards.

Man is safest and most content when he is employed in his routine of work and rest. It is when he makes his periodic departures from this ordered path, in the interest of refreshment, and enters the busy highways and the unaccustomed byways of existence that he risks life and limb and the peace that comes with understanding.

The traumatic toll of the week-end highway and the tragedies of bathing beach and swimming hole are familiar phenomena; a few other major and many minor risks to health and to peace of mind are ready to trap the unwary vacationer. A few of these, and ways to avoid them, are listed by the National Travelers Aid Association, which stands ready to rescue the traveler in trouble, but hopes that he can by-pass it.

Among other things, the traveler is cautioned to carry identification papers at all times — which is particularly important in case of sickness; to make and confirm reservations; to take more money and less baggage than seems necessary; to have a clean bill of health before traveling; to carry simple medical supplies suitable for the immediate care of cuts, burns and insect stings; and when a baby is included in the party, always to have extra rations for him.

Three specific warnings might be stressed, in addition to the cautions contained in the Travelers Aid list; they are especially for vacations in the country. Avoid trifoliate shiny-leaved shrubs or vines; avoid more than moderate direct exposure to the sun, and avoid drinking any water the source of which is unknown. All these things the traveler may do, and commend himself to the care of St. Christopher.

RADIOACTIVE DIGITOXIN

First studies of radioactive forms of digitoxin in human patients show that it is retained in the body longer than was previously thought. This retention of the drug probably accounts for its cumulative effect and suggests caution in the prolonged treatment of patients. Although digitoxin was first isolated seventy-five years ago, little is known of its action on and its disposal by human tissues. A reason for this is the minute dosage and the difficulty of detection in the body by ordinary chemical means.

A method of growing radioactive foxglove plants has been developed in the "atomic farm" of the University of Chicago. Foxglove was raised in air containing radioactive carbon 14, in the form of carbon dioxide. The "tagged" carbon atoms were taken up by the plant, subsequently being present in the purified digitoxin derived from it. By tracing the radioactivity, one can follow not only the

digitoxin but also the chemical degradation compounds occurring in the body and its tissues.

At the University of Chicago Medical Center radioactive digitoxin was given to 4 patients with heart disease. The labeled drug and its breakdown products could be detected forty to seventy-four days after a single dose. Digitoxin could be detected in the blood as long as twenty-four hours after a single administration. The major route of excretion is by the kidneys, a finding in controversy with previous reports. Ten per cent or less leaves the body unchanged; the rest is broken down by action of body tissues. The greater the dose, the greater the amount of initial excretion.

Three members of the London Commission on Sewers have died from exposure to the worst of atmospheres, in their official examinations under ground.

Boston M. & S. J., *July 14, 1852*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

GOGLIA — Alfred A. Goglia, M.D., of East Boston, died on March 22. He was in his forty-fourth year.

Dr. Goglia received his degree from College of Physicians and Surgeons, Boston, in 1935.

He is survived by his parents, two brothers and a sister.

TALBOT — John E. Talbot, M.D., of Worcester, died on June 5. He was in his seventy-third year.

Dr. Talbot received his degree from Harvard Medical School in 1912. He was a member of the staffs of Worcester Memorial and City hospitals and was a fellow of the American Medical Association and a member of the New England Obstetrical and Gynecological Society.

He is survived by his widow and a sister.

LEONARD — Ralph D. Leonard, M.D., of Melrose, died on May 27. He was in his sixty-sixth year.

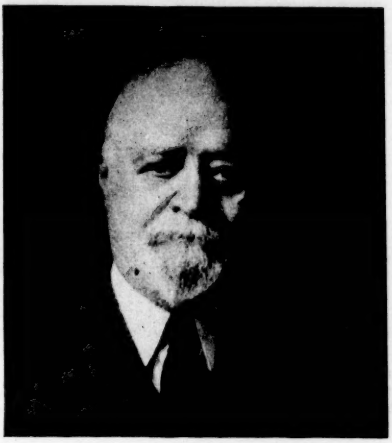
Dr. Leonard received his degree from Harvard Medical School in 1910. He was formerly chairman of the Section of Radiology of the Massachusetts Medical Society, president of the New England Roentgen Ray Society, vice-president and member of the council of the American Roentgen Ray Society and instructor in radiology at Tufts College Medical School. He was chairman of the Melrose School Committee, a fellow of the American Medical Association and the American College of Radiology and a member of the American Roentgen Ray Society, New England Roentgen Ray Society, Massachusetts Trudeau Society, Society of Examining Physicians and American Board of Radiology.

He is survived by his widow, a daughter and a brother.

OBITUARY

CHARLES E. MONGAN

1860–1952



Charles E. Mongan, a native of Somerville, Massachusetts, and a graduate of Somerville High School, received his bachelor's degree at Boston College in 1883, after which he taught school for three years. At the age of twenty-nine he entered Harvard Medical School, from which he graduated in 1892. He received further medical training at Trinity College and the Rotunda in Dublin; he also served an internship at Guy's Hospital in London. With this unusually thorough preparation he entered practice in Somerville, remaining actively at work until two years before his death.

During this long period of active service he established a reputation for uncompromising honesty, devotion to the welfare of his patients and an interest in the medical, social and economic problems of his fellow practitioners. Having a special aptitude for organization, he was for many years a valued delegate from the Massachusetts Medical Society to the American Medical Association and took an active part in the debates of the House of Delegates. Interested in raising the standards of obstetric practice, Dr. Mongan organized the group that founded the New England Obstetrical and Gynecological Society; he was the Society's first president.

He was president of the Massachusetts Medical Society in 1935 and 1936.

Dr. Mongan was for many years a member of the Medical Board of Somerville Hospital, and a senior surgeon there; his thorough and detailed care is

attested to by a large group of loyal patients and friends. His advice was often sought and was freely given to various groups in his city.

At the close of a long, useful and happy life he is survived by his widow, two sons and two daughters.

BOSTON MEDICAL LIBRARY

REPORT OF THE PRESIDENT

To the Trustees and Fellows of the Boston Medical Library:

When I was asked to become president of the Boston Medical Library I was very reluctant to do so. I had served only one year as trustee and believed that I knew very little about running a library. In the six years since then I have learned a great deal, thanks to the very cordial attitude of the Librarian and the Director, to whom I take this opportunity of expressing my gratitude. I found I had no conception of the position the Library occupied in the field of medicine. I soon realized that it was not merely a collection of books put upon the shelves as they came off the press — not merely a collection of periodicals — but a careful selection of the works of the great men in medicine from 1200 A.D. down to the present time — the third largest collection of medical literature in the country, numbering about 200,000 volumes and 135,000 pamphlets. Here could be found over 800 works of authors before 1500, the largest collection of Incunabula in a medical library in the United States, as well as medieval and renaissance manuscripts, many written on vellum, and a splendid collection of medical and scientific Hebraica and Judaica.

This collection of rare books was acquired largely by gift and is sustained by the income from legacies left by thoughtful well-wishers of the Library, representing, I discovered, about half the endowment of the Library. This tremendously valuable collection is today much used by scholars but is most inadequately and unsafely housed.

The general collection of current medical literature was growing at the rate of about 3000 volumes a year, and the Library was taking more than 500 periodicals. The circulation of books to members and others amounted to approximately 32,000 and about 7100 persons attended its reading room.

All this looked good, but when I inspected the treasury the picture changed. The income available for running expenses was barely $30,000 a year. How could one run a library of this caliber on $30,000 a year? The faithful staff was accomplishing much against great odds and needed additional help in both technical and housekeeping departments.

This is where the Massachusetts Medical Society came to our rescue with its generous grant of $5.00 from each member's dues. This gave us an additional $25,000 or more a year and helped us to do many things. We were able to clean up a little, have more space in the Deposit Library and transfer many volumes there and others to the storage warehouse. We were able to hire additional personnel and improve the service.

At any rate the use of the Library has increased. The circulation has increased from 31,928 in 1945 to 70,296 in 1951, a gain of over 38,000, or almost 50 per cent, in six years. The attendance in the reading room has also nearly doubled.

I like to think that this means that the physicians of the Commonwealth are more appreciative of what the Library has to offer. At least the Library is more talked about. But we do not owe the increase in use to doctors alone. Scientific and technical workers in commercial laboratories and pharmaceutical houses are cognizant of our wares and are frequent visitors.

In this time the number of volumes has grown to 215,894 and over 154,987 pamphlets — a gain of over 15,000 volumes and 20,000 pamphlets. We now receive 1093 periodicals against 578 in 1945, many of them foreign, even including Russian. There are also at least 50,000 items not cataloged.

While the Library has been growing in volumes, its house has not kept pace. Unfortunately, when the stack block was built the money gave out, and only two tiers of stacks were built. Five more should be completed, and they are very urgently needed. This would save the expensive rental of space in the Deposit Library, as well as speeding up the delivery service.

Then, too, library methods and uses have changed, and the building is not arranged to conduct the business of the Library in the most efficient manner. For instance, there is no service elevator in the stack block, — the passenger elevator is inadequate, — the toilet and wash-room arrangements are antiquated, and the approach and stairways are unattractive. The Director's office and workroom are distant from the cataloging room, and both are far removed from the stacks.

Bearing all these things in mind, the Trustees have caused a survey (financed entirely by voluntary contributions) to be made by the same firm of architects that remodeled the Massachusetts Medical Society building. They have made their report with their tentative suggestions, and Dr. Allen, chairman of the Committee having this in charge, will tell you something about it later. I sincerely hope that some way may be found to implement these improvements.

We have here a really great medical library, rich in resource material, adequate in current medical literature and well supplied with periodicals, both domestic and foreign. The Director estimates the

value of the books and pamphlets to be well over $1,000,000, and I suppose we own pictures and works of art worth over $100,000.

Every physician in Massachusetts ought to be proud of this remarkable institution and should be anxious and willing to support it. Even if no alterations are made in the building its income from invested funds, the Massachusetts Medical Society contributions and the dwindling fellowship dues is not enough to carry it on as it should be done. It seems incredible to me that doctors are unwilling to contribute $15.00 over and above their Massachusetts Medical Society dues to become fellows of the Library. The Fellows constitute the legal corporate body of the Library. They are the custodians of the various funds left for special purposes, and exercise sole voting power. Such a corporate body must always exist, and any future disposition of the Library rests in its hands. Is it not wise as well as economical to spread the responsibility as widely as possible? I think every attempt should be made to increase our membership. An effort should likewise be made to increase the professional fellowships, of which there are about forty. Every hospital of any size in the Commonwealth ought to have a professional membership, and an effort should be made to interest our users among the laboratories, scientific establishments and pharmaceutical houses and insurance companies to join us in this category, where we have now only three. We have only six general hospitals outside the Greater Boston area that are professional members.

Because I am certain that six years is enough for any one man to hold such an important office I am a bit sorrowfully retiring from the presidency. I want to take this opportunity to thank you for your confidence in me in asking me to head the Library for two successive terms. I have enjoyed the service. My association with the Trustees, the Librarian, the Director and the Library Staff has been most cordial, and I thank them most heartily for their loyal support. I have endeavored to make the Library and its treasures better known to the medical profession. Its problems have been a challenge, and although they are by no means solved, there is no cause for gloom.

I have great faith in the Library. I shall always maintain my great interest in it. In the competent hands of my successor I see great promise for the future.

WALTER G. PHIPPEN, M.D.

CORRESPONDENCE

A SLIGHT DISAGREEMENT

To the Editor: I should like to comment on the article published in the *Journal* of November 1, 1951, entitled "Two Centuries of Service — What of the Next?" by Dean A. Clark, M.D.

I have taken the trouble to familiarize myself with Dr. Clark's background in the United States Public Health Service in the Federal Office of Vocational Rehabilitation as medical director of the Health Insurance Plan of Greater New York, as general director of the Massachusetts General Hospital and most recently as a member of the Truman-appointed "Commission on Health Needs of the Nation." Finally, I have reviewed a number of the articles he has written in the last ten years, in addition to the article in question.

Considering Dr. Clark's background it is not difficult to understand his philosophy. However, I find myself in sharp disagreement with it. I am confident that I express the sentiments of a substantial segment of the medical profession and the public in expressing this disagreement. Dr. Clark is a clever writer as is well exemplified in the widely publicized "Clark Report," recently prepared by him and his staff for the Senate Sub-committee investigating voluntary medical care plans throughout the country. In his address delivered on the two hundredth anniversary of the founding of the Pennsylvania Hospital, of which his article is a copy, Dr. Clark summarizes his opinions about the way medicine should be practiced in this country in the future.

In essence, his thesis is that the future role of medicine in this country should be determined by the hospitals under "lay" control. Hospitals, not doctors, are to be responsible for providing all phases of medical care; preventive, curative and rehabilitative, inpatient and outpatient, to all economic segments of the public. The doctors doing the work are to be the salaried employees of these hospitals, with a closed-staff arrangement. The hospitals are to render the bills to the patients for all medical services, and the hospitals, not the doctors, are to decide how much these services are worth.

One cannot help wondering if Dr. Clark understands the full meaning of this formula he has derived. The system he proposes would naturally mean the end of medicine as it is now understood. The physician–patient relation would be meaningless, for his plan contemplates the pure institutional practice of medicine. The fee-for-service basis of medical practice would no longer exist. That this proposed contract sort of practice would be unethical, and has been so defined by the American Medical Association, bothers Dr. Clark not in the least. That the citizen's right of privately contracting with the physician of his own choosing for his services would be destroyed matters not to Dr. Clark. That this system would embrace all that is evil in political medicine by making staff appointments the patronage of a hospital board, many of which are politically controlled, is apparently no cause for alarm to him. Worst of all, Dr. Clark attempts to deceive physicians into believing that his plan would not inevitably lead them down the road to state socialism.

In answer to certain problems, primarily facing the hospitals of this country, Dr. Clark in his own ivory tower proposes a plan that most certainly would destroy American medicine. That his philosophy clashes sharply with traditional American principles must be obvious to the most casual observer. That his scheme is socialistic in design can be readily discerned by an analysis of his accompanying arguments.

If one studies the article in question and strips away the persiflage, the ambiguous statements, the rhetoric and the false logic, the cold hard fact remains that Dr. Clark is attacking free enterprise, for which he would substitute authoritarianism. In consonance with his background, Dr. Clark speaks not as a practicing physician but rather as a politician, an administrative bureaucrat, a social planner.

Purposely, or not, the technic that Dr. Clark employs follows the familiar pattern adopted by cannibalistic politicians the world over. The key to their formula is to get a free people to transfer their individual rights and responsibilities to some central authority of presumed supreme intelligence and benevolence. The first step must frequently be done gracefully by obtaining the transfer at a local level and to bodies in which the people already have trust. In the present case, the people are asked to transfer their right of private contractural agreement with their physician to a third party — the hospitals, their associations and their insurance companies. Clearly written in the history of many nations is the lesson of what is to follow. The further transfer of authority to higher and higher levels sought by omnipresent power-seeking politicians meets with continually lessening resistance on the part of the individual because the individual no longer controls his own destiny. Regardless of Dr. Clark's own particular motives, thinking Americans must be made cognizant of the ultimate catastrophic effect of what he proposes.

The right of private contractural agreement is a keystone of liberty. Many and devious are the ways in which these basic American principles are being undermined. If Americans would preserve a free way of life and maintain and improve their standard of living and health, they must resist all schemes, of whatever origin, that would destroy their fundamental individual rights and liberties.

For the sake of the art and science of medicine in this country and the world Dr. Clark's proposal must be recognized for what it is. It is the responsibility of physicians to create the future role of medicine in this country. Medicine is their business, and they alone are to be held accountable for it. It is their further responsibility to behave as true statesmen in these trying times and not to allow themselves or the public to be misled by the demagoguery of the professional politician, lay or medical. Only in this way can they hope to serve the best interests of the people.

PHILIP W. SMITH, M.D.
Marion, Ohio

Dr. Smith's letter was referred to Dr. Clark, who offers the following reply:

To the Editor: It seems to me that Dr. Smith has misinterpreted my meaning in a number of regards. In the first place, my article, it seems to me, does not propose any new form of "lay" control over medicine as Dr. Smith seems to believe it does. It merely emphasizes the fact that throughout history, by its very nature, the practice of medicine has always been a matter in which the public has a vital stake and over which, therefore, the public has always maintained a certain control. The mere fact that doctors are licensed by public authorities, for example, indicates the nature of this relation.

Secondly, my suggestions about the functions of hospitals do not in the least imply, I believe, that hospitals are to dominate the practice of medicine. On the contrary, I was attempting to show how hospitals can be more effectively and economically utilized in medical practice to further the general improvements of preventive medicine and rehabilitation, as well as diagnostic and curative medicine. Nowhere in the article is there any attempt to define the relation that should be maintained between medical staffs and hospital trustees. The one section that might be so interpreted is the discussion of salaried medical practice. This section was not intended to imply that all physicians should be salaried but rather that there should be no serious objection to such a system if satisfactory arrangements could be made with the institution at which they are working.

Finally, I cannot accept Dr. Smith's interpretation that the article proposes authoritarianism or socialism. Indeed, the principal plea of the entire piece is for more open-minded and impartial consideration by both the medical profession and the public of the various difficult problems facing medicine today. It still seems to me that this is the only rational way to approach these problems, and in this I hope Dr. Smith will agree. Arbitrary stands taken either by the profession or by the public can do nothing but harm. I am convinced that sound development in a rapidly changing scene can be accomplished if all parties are willing to approach the problems with reason and patience.

DEAN A. CLARK, M.D.
General Director, Massachusetts General Hospital
Boston, Massachusetts.

BOOK REVIEW

A Translation of Galen's Hygiene. (De Sanitate Tuenda). By Robert M. Green, M.D. With an introduction by Henry E. Sigerist, M.D. 8°, cloth, 277 pp. Springfield, Illinois: Charles C Thomas, 1951. $5.75.

Dr. Green has for the first time rendered into a modern language Galen's work on personal hygiene. The translation has been made primarily from the Greek and Latin text of Kuhn (Leipzig, 1815) compared with the translations of Linacre (1823) and Robert Koch (1923). The text is preceded by a short biography, translated by Dr. Sidney Licht from LeClerc. The printing is done with a good, large type on a non-glare paper, and the publishing as a whole is excellent. The book is recommended for all medical-history collections.

JAMES F. BALLARD

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Surgical Practice of the Lahey Clinic. By staff members of the Lahey Clinic, Boston. 8°, cloth, 1014 pp., with 509 illustrations. Philadelphia: W. B. Saunders Company, 1951. $15.00.

This new volume from the Lahey Clinic in Boston is issued almost ten years since the publishing of the first volume from the Clinic and practically constitutes a second series. A large number of papers have been contributed by members of the staff. The material is divided into eleven special sections and one miscellaneous section, including the thyroid gland and neck, the esophagus, lungs and heart, the stomach, duodenum and intestines, the biliary tract, spleen, adrenal gland and pancreas, breast, pelvis, bones and joints, brain, spinal cord and nerves and anesthesia. There is a comprehensive index, and the publishing is excellent. The book should be in all medical libraries and available to all surgeons and other specialists.

Clinical Laboratory Diagnosis. By Samuel A. Levinson, M.D., Ph.D., director of laboratories, University of Illinois Research and Educational Hospitals, and professor of pathology, University of Illinois College of Medicine; and Robert P. MacFate, Ch.E., M.S., Ph.D., chief, Bureau of Laboratories, Chicago Department of Health, and assistant professor of pathology, University of Illinois College of Medicine. Fourth edition. 8°, cloth, 1146 pp., with 221 illustrations and 13 plates. Philadelphia: Lea & Febiger, 1951. $12.00.

This edition of a standard reference book has been revised to bring it up to date. The authors have had the assistance of Louis R. Limarzi, M.D., Clarence W. Muehlberger, Ph.D., and Marion Hood, Ph.D. The chapters on hematology, and on toxicology have been rewritten. New material has been added on the biologic assay of the antibiotics, blood chemical analysis, using the spectrophotometer, electrolyte balance and the determination of the various Rh factors. There is a good index and the book is well published. It is recommended for all medical libraries.

NOTICES

ARMY MEDICAL SERVICE POSTGRADUATE COURSES

The Army Medical Service will conduct 17 short postgraduate courses in surgery, psychiatry and other subjects of major medical importance during the last six months of 1952. The instruction is open to both military and civilian physicians. The courses will be given at six large Army teaching hospitals and the Armed Forces Institute of Pathology in Washington, D. C.

Applications from Army medical officers on active duty and full-time Civil Service physicians at Army installations should be forwarded to the Office of the Surgeon General, Department of the Army, Washington 25, D. C. (ATTENTION: Career Management Branch, Personnel Division).

Reserve medical officers should apply to the Army area commander, and National Guard physicians should write the National Guard Bureau in Washington. Civilian physicians in the Federal service or in private practice should apply to the appropriate hospital or installation commander.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS

The sixth annual meeting of the American Society for the Study of Arteriosclerosis will be held at the Hotel Knickerbocker, Chicago, on November 9 and 10. The complete program and the proceedings will be published in the September issue of *Circulation.*

(*Notices concluded on page xi*)